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A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

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Clinical Background of Dextri-Maltose

Continued down from 1911

1922

In the treatment of diarrhea, "The sugar is added gradually as conditions admit, some sugar other than milk sugar or cane sugar being used, preferably dextrin and maltose."—*H. E. Small: Diarrhoea in bottle-fed infants, J. Maine M. A. 12:154-158, Jan. 1922.*

1922

"The use of other soluble carbohydrates other than lactose for milk modifications are very good. Some believe the addition of dextrose or dextri-maltose makes the casein curd softer and easier to digest. This is questioned, but all agree that in cases of malnutrition, where the patient is intolerant to lactose and cannot get the benefit needed from the fat in the diet that the dextri-maltose is invaluable as it is the easiest sugar to digest, and can be immediately used for energy production without undergoing further change."—*E. G. Padfield: Remarks on infant feeding, J. Kansas M. S. 22:97-101, April, 1922.*

1922

In the treatment of intestinal disturbances, "Practically the method followed has been that employed when beginning simple dilutions, starting with ¼ or ⅓ albumin milk, diluting with water and sweetening with saccharin, except that the food has been strengthened more rapidly. Dextri-maltose No. 1 is added as soon as possible to reinforce the food value as albumin milk alone in full strength values but 13 Calories per ounce."—*S. D Giffen: The feeding of infants based on recent experience, Ohio St. M. J. 18:829-833, Dec. 1922.*

1922

". . . maltose is usually better tolerated by babies than either lactose or dextrose. Advantage may be taken of this property of maltose, by developing as rapidly as possible the starch-digesting functions of infants with low degrees of sugar tolerance, since the slow conversion of starch into maltose by the action of diastase promotes the object in view most satisfactorily."—*E. Pritchard: The Physiological Feeding of Infants and Children, Henry Kimpton, London, 1922, p. 365.*

1922

"A large percentage of the sugars ingested with the food is lost through fermentation. Lactose is most readily affected by the intestinal bacteria, undergoing lactic acid fermentation which gives the stool of the breast-fed infant its characteristic sour odor. In bottle-fed infants this fermentation is likely to exceed the limits which occur in natural feeding and an acid diarrhea frequently results from the fermentation of the lactose. If the fermentation is not promptly controlled serious disturbances may result. Maltose does not ferment as readily as lactose while cane-sugar does not undergo lactic acid fermentation at all. Dextrin and starch exert an inhibiting action over intestinal fermentation and are therefore used to 'correct' this tendency in the bottle-fed infant."—*C. S. Rau: Diseases of Children, Boericke & Tafel, Phila., 1922, p. 54.*

1922

In the treatment of marasmus, ". . . ten ½ oz. feeds of albumin milk with 3 per cent. carbohydrate altogether made up with dextri-maltose are administered in the twenty-four hours at intervals of two hours: also as much water as the child wants in between feeds. . . . If the weight has been steadily increasing the dextri-maltose is then gradually and cautiously increased to 5 per cent., and after a week or two (or four to five weeks on albumin milk altogether) a return can be cautiously made to a suitable ordinary milk-mixture if all be well."—*B. Myers: Practical Handbook on the Diseases of Children, H. K. Lewis & Co., London, 1922, p. 160.*

1922

"Maltose, either in the form of malt soups or in combination with dextrin, 'dextrimaltose,' can be substituted for milk-sugar.

"It is very much more easily assimilated than other sugars. It will, however, break down more readily. It should be weighed in determining the proper amount to add."—*R. S. McCombs: Diseases of Children for Nurses, W. B. Saunders Co., Phila., 1922, p. 405.*

1922

"If there is any tendency to sugar fermentation, use a preparation with a high dextrin and relatively low maltose content, as Mead's dextri-maltose."

"If it is desired to feed an unusually large amount of sugar to a baby, it is well to use a maltose-dextrin preparation, as in this way there is less danger of bringing about sugar fermentation than if lactose were used."

In marasmus, "When the stools have become smooth and salve-like, carbohydrate, in the form of dextri-maltose, may be gradually added up to the limit of tolerance."—*L. W. Hill: Practical Infant Feeding, W. B. Saunders Co., Phila., 1922, pp. 206, 231.*

1922

In the treatment of decomposition, "As a rule it is best to start with 2 to 2½ or 3 ounces of albumin milk to the pound weight in 24 hours; the sugar to be added is in the form of a maltose-dextrin mixture. One should never delay too long in adding this."—*C. G. Grulee: Infant Feeding, W. B. Saunders Co., Phila., 1922, p. 265.*

1922

In decomposition, "The period of repair may be shortened by giving suitable additional food; the best, probably, being buttermilk to which carefully regulated proportions of dextrin and maltose preparations or malt soup are added."—*E. Feer: Text-Book of Pediatrics, J. B. Lippincott Co., Phila., 1922, p. 284.*

1922

Regarding treatment of the marantic infant, "After the intolerance to sugar has been overcome a carbohydrate, preferably Dextri-maltose, may be added."—*C. S. Rau: Diseases of Children, Boericke & Tafel, Phila., 1922, p. 427.*

1922

In spasmophilia "Dextri maltose is the best sugar to use in these cases, in the proportion of 6 to 8 per cent."—*J. H. Reading, Jr.: Spasmophilia, Hahneman. Monthly, pp. 403-411, July, 1922.*

1922

In pylorospasm, "Before the food is given, the stomach is carefully washed until the washings return clear. The food is then given through the tube before it is withdrawn. The food given in these instances is practically always a mixture of albumin milk and a dextrin-maltose combination, a quantity sufficient to meet the needs of a child of like age and weight without gastro-intestinal disturbance."—*C. G. Grulee: Treatment of pylorospasm in infants, J.A.M.A. 78:1183-1184, April, 22, 1922.*

1922

"Malt sugars are of value and are better than milk sugar in increasing nutrition and adding weight."—*W. L. Carr: A group of difficult feeding cases, Arch. Pediat. 39:715-719, Nov. 1922.*

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The Journal of Pediatrics

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Original Communications

THE THYMUS GLAND AND THYMIC SYMPTOMS

AN INVESTIGATION OF 1,074 NEWBORN BABIES

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THE thymus gland and its relationship to a certain more or less definite symptom-complex in the newborn and babies in early infancy presents a number of problems for consideration and study. This question has been discussed from various angles by many observers in different countries, particularly in the United States. Opinions are quite divergent. One cause for this difference of thought is the confusion that has arisen because of attempts to link so-called simple hypertrophy of the thymus itself with the constitutional diathesis, status thymicolymphaticus. Furthermore, the causation of the occasional sudden death that occurs in infancy and early childhood for which no clinical or anatomical basis can be found is traditionally associated with the thymus and termed "thymic death." Marine,[1] in reviewing the status lymphaticus problem, says that he accepts the views expressed by Friedleben, Paltauf, Wiesel, Hart, Ohlmacher, Thomas and others, that there is no known disease entity in which the thymus occupies the central or causal rôle. He says that the terms, "thymic death," "thymic asthma," "status thymicus," and "status thymicolymphaticus," are misleading. Other writers correlate "thymic death" with status thymicolymphaticus. We feel that the thymus syndrome which occurs in newborn infants, and with which we are concerned in this present investigation, bears no relationship to the status thymicolymphaticus syndrome; the latter is a systemic disease affecting not only the thymus gland but also the spleen, intestinal follicles, lymph nodes, tonsils, Waldeyer's ring, Peyer's patches, and bone marrow; and it is associated with hypoplasia of the cardiovascular system and probably of the chromaffin system and gonadal glands (suprarenal cortex, interstitial cells of the testes and ovaries). When such an individual

From the Pediatric Service of Dr. Robert A. Schless, Jewish Hospital, Philadelphia.
Read before The Philadelphia Pediatric Society, November 14, 1933.

grows older, a distinctive body constitution is usually also associated therewith. The infants that have an enlarged thymus gland do not, however, belong to any particular constitutional type, except that a number of observers claim that the large well-nourished baby is more prone to suffer from hypertrophy of the thymus. Cole[2] doubts the diagnosis of "thymic death" and considers the diagnosis of enlarged thymus an "alibi diagnosis"; he states that there is little evidence to show that the thymus plays any pathologic rôle. "Certainly it is so rare," he says, "as to be practically negligible in its importance in pediatric practice." Hammar,[3] as a result of an investigation of a series of so-called "thymic deaths" in children, found no marked enlargement of the gland, no definitely characteristic pathologic or morphologic changes, nor any basis for assuming that death was due to an increased or decreased function of the gland.

The weight and size of the thymus are subject to great fluctuations, and for this reason it is very difficult to set up an average weight or even to state a limit beyond which the gland becomes pathologic. In other words, the size and weight of the thymus gland vary so much within normal limits that it is only when an extremely large gland is found at autopsy that the condition can be called abnormal. It certainly appears that the size and weight of the thymus gland are closely related to the general state of nutrition of the infant, and that with a loss of weight there is a corresponding loss of gland-substance in the thymus; nevertheless, we cannot speak of an exact relationship between size of the thymus, age, body weight, or state of nutrition. In this connection, the thought projects itself as to whether the frequently made observation that hypertrophy of the thymus is usually found in the large infant is not due to the fact that a well-nourished, large infant would proportionately have a greater amount of thymic tissue. This physiologically large thymus might in turn be diagnosed as the cause of any symptoms related to the so-called "thymus syndrome." According to Finkelstein,[4] an anatomical diagnosis of hypertrophy of the thymus should only be made when, in the presence of good nutrition, the weight of the gland is above 20 gm. in the first year and above 25 gm. in the second year. Marine[1] states that "anatomists in general agree that the absolute weight of the thymus gland increases rapidly up to the end of the second year of life, and then changes but little until the seventh year, when it again increases slightly, to fall off again at about the eleventh year." Hammar[5] found the increase in the size of the gland after the second year largely due to an increase in the interlobular stroma.

There is a great variation in observations as to the supposed normal weight of the thymus gland at different ages. This is due to the fact that most terminal illnesses that last over twenty-four hours cause a reduction of the weight of the thymus; the gland of a two-week-old

infant who has been sick for a week will be smaller than the gland of a similar sized and aged infant who has been sick for only one day before death. In other words, this shrinkage of the thymus is probably a part of the general involution resulting from disease and inanition. The correct weight of the thymus gland is best obtained where the individual died an accidental death, with no preceding illness. Boyd[6] says, "with the exception of tumors of the thymus, leucemia, and exophthalmic goiter, the weight of the thymus is reduced from whatever illness has caused death, when said illness has lasted twenty-four hours." Friedleben[7] found experimentally, as far back as the middle of the nineteenth century, that the thymus gland can shrink to one-half its former size in the first days of hunger; hence, for the determination of normal weights, he used only glands that were obtained from cases of sudden death. Based on seventy-two cases, he found the average weight of the gland of full-term newborn babies to be 14 gm. Friedman,[8] in a recent article, states that the normal average weight of the thymus gland of a newborn infant is about 10 gm. but this is merely his impression, and not based upon actual weight determination. Boyd[6] states that although the variability of the thymus gland is high at all ages, it averages approximately 20 gm. at birth, 28 gm. at eight years, birth size at the age of sixteen, and gradually decreases to about 15 gm. in late adult life. On the other hand Clark,[9] in an analysis of forty thymus glands from infants, twenty of whom were in the first trimester of life, found that the gland at birth averaged 3.4 gm. and rapidly decreased during the first six months, after which a gradual secondary enlargement ensued. *The concept of a pathologic thymus arose, therefore, from misconstruing the normal prominent thymus found at autopsy following sudden deaths for a constitutional abnormality; and from construing the small involuted thymus resulting from inanition as the normal thymus.* The most commonly quoted average weights of the thymus gland in relation to age are those of Hammar,[10] which represent the weights of the thymi of individuals who died from accidents, homicide, or suicide.

TABLE I

AGE	WEIGHT IN GM.
Full-term newborn	15.15 gm.
1- 5 yr.	25.86 gm.
6-10 yr.	29.42 gm.
11-15 yr.	29.41 gm.
16-20 yr.	26.24 gm.
21-25 yr.	21.05 gm.
26-30 yr.	19.54 gm.
31-35 yr.	20.17 gm.
36-45 yr.	19.03 gm.
46-55 yr.	17.32 gm.
56-65 yr.	14.30 gm.
66-90 yr.	14.06 gm.

Hammar, who carefully estimated the exact amount of parenchyma minus the fat and connective tissue and counted the number of Hassall's corpuscles, found the thymus enlarged in only two of fourteen cases of "thymic death." Boyd says that a graphic presentation of Hammar's data indicates that the parenchyma decreases sufficiently after puberty to lower the total weight of the thymus, even though the fat and connective tissue are increased in amount.

Table II is said by Marine to represent the most commonly quoted average weights of the thymus gland in relation to age.

TABLE II

WEIGHT OF THYMUS IN GRAMS

AGE	FRIEDLEBEN 1858	VON SURY 1908	HAMMAR 1906	SCHRIDDE 1923	BRATTON 1925
Newborn	14	14	13	13	11
1-5 yr.	(1-9 mo.)-20 (9 mo.-2 yr.)-26	22	23	17	24
6-10 yr.	(3-14 yr.)-26	29	26	20	29
11-15 yr.	..	32	38	25	27
16-20 yr.	(15-25 yr.)-22	..	26	20	..
21-25 yr.	..	..	25	19	..
26-35 yr.	3	..	20	14	..
36-45 yr.	..	..	16	10	..
46-55 yr.	..	..	13	7	..
56-65 yr.	..	..	16	4	..
66-75 yr.	..	..	6	3	..

ROENTGENOLOGIC EXAMINATION

The frequency with which various investigators find enlargement of the thymus gland on roentgenologic examination is subject to a great many variable factors, including: the patient's age when the films were taken; the position in which the individual investigator examined the patient by roentgen ray; the interpretation of the roentgenogram, whether or not it was based upon the anteroposterior view or in conjunction with the lateral view; the moment the pictures were taken, whether only on inspiration, on expiration, or both. Furthermore, Hasley's and De Tomasi's[11] work with rapid x-rays (about five pictures in two seconds, taken on a reel) demonstrates that the thymus gland varies in size, depending upon the phase of the cardiorespiratory cycle in which the picture was taken. Birk and Schall[12] report finding hypertrophy of the thymus gland in only four out of 1,000 newborn infants. Perkins[16] examined 700 children and made a roentgenologic diagnosis of enlarged thymus in thirty, or 4 per cent. Friedman's[8] study of infants under one year, who were radiographed for various reasons, revealed a residual or hyperlastic thymus in less than 5 per cent of those examined. Bliss,[13] in a study of 1,400 newborn infants, found that seventy, or 5 per cent, showed dangerously enlarged thymi. Saupe[14] was only able to diagnose definite hypertrophy of the thymus

in six out of 100 newborn babies that were examined roentgenologically. Mosher[15] found an enlarged thymus gland in 7 per cent of children between the ages of two and sixteen years. Podlasky and Kohn[17] examined 100 consecutive newborn infants, presumably in the anteroposterior position only; thirty-five showed definitely enlarged thymi; none of them, however, showed associated symptoms. Singleton[18] found enlarged thymi in 35 per cent of the newborn; he, however, based his conclusions on roentgenograms taken only in the anteroposterior position. Liss[19] found that in 42 per cent of the infants examined by x-ray within forty-eight hours after birth, there were thymic shadows measuring more than 3 cm. wide; these shadows he interpreted as enlarged and pathologic. Spontaneous retrogression and disappearance of this shadow took place in the majority of these cases; some, however, persisted to the second year. Peterson and Miller[20] found in their series that 43 per cent had enlargement of the thymus gland. Hardy[21] demonstrated enlargement of the thymus gland in 50 per cent of symptom-free infants. Johnston and Howard[22] found from 42 to 50 per cent of normal symptom-free newborn babies with enlarged thymus shadows by x-ray. From a total of 1,074 newborn babies our own figures show 322 infants with enlargement, an incidence of 30 per cent. On excluding from our figures 150 infants that showed +1 (moderate lateral) enlargement, the incidence drops to 16 per cent. The school that claims that the large thymus causes symptoms through pressure, will not object to the elimination of the 150 cases that showed a +1 enlargement, that is, the mildest degree of hypertrophy. However, the group that maintains that the hypertrophied thymus gland causes symptoms through an increased or perverted chemical secretion will not permit the elimination of these 150 cases from our figures, and, for that group, the incidence of 30 rather than 16 per cent would be more acceptable. We see, therefore, that in the medical literature the figures on the occurrence of enlargement of the thymus gland on roentgenographic examination vary from 0.4 per cent to 50 per cent. This denotes considerable difference of opinion, and most important of all, these differences are predicated upon esoteric concepts of normality.

Rudisill,[23] in a study of eighty-eight autopsies at the Children's Memorial Hospital of Chicago between January 1, 1930, and March 1, 1931, found only one definitely enlarged thymus, giving a percentage of 1.1 per cent. The one child in whom he found a large thymus was nineteen months old, and the weight of the gland was 45.5 gm.; this child, however, had no symptoms referable to the thymus or respiratory system. The cause of death was shock and hemorrhage during a two-hour operation for osteomyelitis. Rehyer[24] investigated 200 children, sixty-eight of whom came to autopsy. The chief symptom in his cases was an inspiratory congenital stridor. In most of the cases there were medium-sized, and in several, only small thymus glands. In the cases

showing large thymus glands (45 to 46 gm.), there was no congenital stridor, which, the author remarks, confirms Finkelstein's skepticism concerning the existence of a thymic stridor.

AUTHORS' STUDY

Our investigation consisted in the study of 1,074 newborn infants who were routinely examined by x-ray for enlargement of the thymus gland. These babies were born between January 13, 1930, and April 6, 1932, at the Jewish Hospital, Philadelphia. The number of patients who were actually given x-ray examinations was over 2,000, but we limited our study to those who had lateral x-ray pictures taken as well as anteroposterior, both on inspiration as well as on expiration. Exposures were made with the babies in the recumbent position at skin target distance, that is, 36 inches from the surface of the infant. The pictures were all taken according to the directions of Pancoast and Pendergrass as followed in the Department of Roentgenology at the University of Pennsylvania. When the anteroposterior pictures were taken, the arms of each infant were held above the head; the head was kept exactly straight and in the midline, midway between flexion and extension. For the lateral view, the arms were held downward and backward, and the head was held raised so that the neck was absolutely straight with the body and exactly midway between flexion and extension. This technic is not only superior to the other methods of roentgenography of the thymus gland, but it also gives a correct view of the larynx; so that if buckling of the trachea is seen, it would be due to actual pressure rather than the way the head was held during the taking of the roentgenogram. These babies included private as well as ward deliveries and were all routinely examined by x-ray, irrespective

TABLE III

AGE AT TIME OF ROENTGENOLOGIC EXAMINATION

NO. OF INFANTS	AGE IN DAYS	NO. OF INFANTS	AGE IN DAYS
62	1	10	9
74	2	3	10
53	3	4	11
46	4	4	12
25	5	1	13
15	6	1	14
11	7	1	16
9	8	1	21
		1	3 mo.

of whether or not they had symptoms referable to enlargement of the thymus gland. The majority of the babies was examined during the first week, a very small number during the second week, and only four infants between the second and twelfth week of life.

Out of the 1,074 newborn babies who were examined anteroposteriorly by x-ray, as well as laterally on inspiration as well as expiration, 322, or 30 per cent, were reported to show thymic enlargement. The sexes were almost equally divided, 157 males and 155 females. Almost one-half (142) of the infants who showed enlargement of the thymus gland were first-born.

142 first-born	5 sixth-born
83 second-born	1 seventh-born
47 third-born	2 eighth-born
31 fourth-born	2 ninth-born
7 fifth-born	2 tenth-born

We classified the 322 cases into four groups, the subdivision being based upon the direction and degree of enlargement reported roentgenologically. We assumed that an enlargement of the thymus gland in its anteroposterior diameter, which gave rise to compression, displacement, or other encroachment upon the trachea, was of greater significance than a lateral enlargement, thus favoring slightly the school that claims that "thymic symptoms" are the result of mechanical pressure rather than an excessive thymus secretion. Furthermore, Noback's[25] anatomic studies of the thymus gland in the newborn and early infancy confirm the long-held suspicion that mere enlargement of the thymus gland shown on anteroposterior photography does not necessarily indicate a thymus of pathologic possibilities. He says that "with the initiation of respiration and the resultant expansion of the lungs, pressure is exerted by these organs against the sides of the thymus. This pressure results in a narrowing of the thymus and is evident in children who have lived but one-half hour. With increased expansion of the lungs and resulting increase in pressure upon the sides of the thymus, a flattening of the convex sides occurs and, later, deep depressions are developed. Along with this narrowing of the thymus, an elongation of the gland occurs, and it is extended inferiorly over the surface of the heart. The outline of the thymus in the late fetus and in the stillborn child is similar to that described by many roentgenologists as 'enlarged' or 'hypertrophied.' In this latter, it seems, we have normal glands which as yet have not been fully narrowed by the lungs. It is quite probable that many thymi may retain this broad type for several years and yet not be pathologic." The classification of our cases follows:

Plus 1.—Moderate lateral enlargement of one or both lobes with no compression of the trachea.

Plus 2.—Definite lateral enlargement of one or both lobes with no compression of the trachea.

Plus 3.—Moderate lateral enlargement of one or both lobes with definite compression of the trachea.

Plus 4.—Definite lateral enlargement of one or both lobes with definite compression of the trachea.

Taking the midspinal line as the longitudinal line of departure and a point immediately above the indentation of the right side of the heart with the great vessels as the horizontal line, we measured on the anteroposterior plate taken during expiration, the width of the shadow of the supposed thymus gland to either side of the longitudinal line and above the horizontal line. The shadows that measured more than 1.5 cm. to the right or to the left of the midline, or both, were those which were designated as "definite enlargements"; the shadows that were less than 1.5 cm. wide to either or both sides of the midline were called "moderate enlargements." Practically most of the shadows were of the high type, that is, were above the horizontal line; many of them were distinctly columnar in character, and a few were of the lobated type.

Forty-five of the newborn babies examined showed a +4 thymic enlargement; fifty-one were of the +3 type; seventy-six belonged to the +2; and 150 cases were of the +1 type of enlargement. If we eliminate the 150 cases which belong to the +1 type, that is, babies who showed only moderate lateral enlargement with no encroachment upon the trachea, and in which the roentgenologist recommends as a rule, "No treatment indicated unless symptoms present," there would remain only 172 cases that showed significant enlargement of the thymus gland, an incidence of 16 per cent.

The symptoms usually said to be associated with enlargement of the thymus gland are inspiratory or expiratory stridor (the former being more common), crowing, dyspnea (continuous, intermittent, or paroxysmal during crying or feeding—at times so slight as to comprise noisy rather than difficult breathing), dysphagia, cyanosis (as a rule never continuous), asphyxia, vomiting simulating pylorospasm, choking or brassy coughing (occurring sometimes only during feeding), and rarely, retraction of the intercostal spaces. In marked enlargement, some authors claim that the gland may even be palpable in the suprasternal notch and that there may be a failure of the larynx to move downward during inspiration because it is held up by the thymus gland. Another sign sometimes given is the improvement or disappearance of the thymic symptoms on extension of the head. Those who claim that they are able to detect the thymus gland by percussion report dullness in the second interspace to the right and left of the sternum, usually continuous with cardiac dullness. Holt and McIntosh[26] state that "the diagnosis of thymic enlargement is often wrongly made on clinical evidence. In the majority of patients who have been brought to us with this diagnosis already made on the basis of stridor, cyanotic spells, or convulsions, some other condition has been responsible—most commonly deformity or disease of the larynx, less often atelectasis, congenital malformation of the heart, or even tetany." As a matter of fact, the conditions that one

should always consider when a diagnosis of thymic enlargement is made are: (1) atelectasis; (2) cerebral hemorrhage; (3) congenital heart disease; (4) laryngeal anomalies or infections; (5) bronchitis or pneumonia; (6) large mediastinal glands; (7) retropharyngeal, peritonsillar or cervical abscess; (8) asthma; (9) laryngospasm or tetany of the newborn; (10) congenital laryngeal stridor, the diagnosis of which condition, we believe, is not made sufficiently often; (11) micrognathia; (12) large adenoids; (13) breath-holding; (14) macroglossia; (15) tongue-swallowing; or (16) foreign body in pharynx or larynx.

Tucker[27] says that "in an infant the entrance to the larynx is at an angle from behind forward and downward toward the glottic lumen. With descent of the larynx, as the child cries, the epiglottis assumes a more nearly vertical position, making the axis of the lumen at the entrance of the larynx more nearly in the line with the subglottic larynx and trachea. *An increase in this angle of entrance into the larynx in certain types of infantile larynx may become one of the factors in the production of so-called congenital stridor.*" He states further that "a subglottic diameter of 4 mm. is to be considered an actual congenital stenosis when it is found in an otherwise normal infant." This, it seems to us, should be added as another possible cause of the so-called "thymic syndrome." That stridor is probably one of the most common symptoms of so-called thymic enlargement is emphasized by Tucker[27] when he says that "probably the most frequent condition in which the laryngologist is asked to give an opinion in infants is so-called congenital stridor . . . and the most common abnormality found is the exaggerated infantile type of larynx." He also found papillomata and congenital webs of the larynx and, in one case, a broad-based, flaccid epiglottis which was sucked into the glottis, as conditions which produced stridor in the newborn. In this connection, we are purposely quoting in detail two cases which Tucker[27] reports under the heading "Congenital Stridor and Enlarged Thymus."

Case 1.—"Infant, six months old, congenital stridor since birth with only slight dyspnea. X-ray was interpreted as showing enlarged thymus. Laryngoscopy showed bilateral posticus paralysis of larynx. Bronchoscopy showed evidence of tracheal compression. Tracheotomy relieved the symptoms."

Laryngeal paralysis is certainly not caused by enlargement of the thymus.

Case 2.—"Four-month-old infant, congenital stridor and retraction of suprasternal notch and tip of sternum since birth. The x-ray showed positive evidence of thymic enlargement; a series of x-ray treatments were given, and the *enlargement disappeared, but the stridor persisted, and the dyspnea increased.* The laryngoscopy showed the mucous membrance of the larynx inflamed but the larynx normal. *On inspiration there was marked indrawing of the aryepiglottic folds and arytenoids. As the symptoms increased, a tracheotomy was done.*"

"In this child," Tucker comments, "the symptomatology was primarily due to the condition of the larynx although there was definite

evidence of enlarged thymus. The dyspnea was not relieved because there was a congenitally small larynx, the subglottic measurements being 4 mm."

Two cases of our own illustrate the pitfall of error that one is liable to in the interpretation of stridor in its relationship to a roentgenologically enlarged thymus.

Case 1.—H. K., female, five days old; three weeks premature. Birth weight 6 pounds, 3 ounces. Routine x-ray picture of chest revealed no enlargement of thymus gland. At two months of age the baby developed a marked laryngeal stridor which disappeared only when asleep. X-ray examination of chest at that time was reported as follows: "There is a moderate degree of nodular enlargement of the thymus. This displaces the trachea to the right. The trachea is normal in size. The heart, lungs, and diaphragms present normal appearances." Against the authors' advice, and following the recommendation of the roentgenologist, the baby was subjected to five x-ray treatments, following which another x-ray picture of the chest was taken (one month after the above quoted report). The report follows: "My examination shows complete recession of the enlarged thymic shadow. The trachea at this time occupies the central position, there being no evidence of displacement or compression. The heart is normal in size, shape, and position. The lungs present a comparatively normal appearance."

In spite of the x-ray treatments, which brought about a shrinkage of the thymus gland and a return of the trachea to its normal position, the stridor continued, evidently not due to the enlarged thymus reported, but to laryngeal stridor per se. The roentgenologist was apparently satisfied in that he had brought about a normal thoracic picture; however, the child's stridor continued until she was past one year of age.

Case 2.—M. H., male, birth weight 8 pounds, 5 ounces. Chief complaint: whistling stridor since birth. Physical examination showed nothing to account for this. Despite advice to the mother that the symptom would probably disappear as the child grew older, she, having heard the gospel of the enlarged thymus from her friends, insisted upon an x-ray picture. This was made and the roentgenologist's report follows: "There is marked bilateral enlargement of the thymus gland. There is slight compression upon the trachea." This baby was subjected to two x-ray treatments without any relief. At eight and a half months the child still showed the same type of whistling stridor although the roentgenogram of the chest no longer revealed any thymic enlargement.

The following two cases are examples of the growth of the thymus gland after birth:—

Case 3.—C. D., male, was routinely examined by x-ray five days after birth, and the picture showed an enlarged thymus of a + 2 type. As the baby had no symptoms, he was not subjected to treatment. At seven weeks of age he was admitted to the hospital on account of a febrile condition, and his chest was again examined by x-ray and showed a + 4 enlargement of the thymus gland. In spite of this marked enlargement, the baby showed no symptoms relative thereto and, had it not been for the accidentally taken picture, one would never have known that the gland enlarged from a + 2 to + 4 type.

Case 4.—J. A., male, one day old. Routine x-ray examination of the chest showed a + 2 enlargement of the gland. The roentgenologist's report follows: "Thymus showed distinct lateral enlargement with some encroachment upon the trachea posteriorly." Two and one-half months later, he was readmitted to the hospital on account of symptoms of pneumonia. The x-ray picture of the chest showed a + 4 enlargement of the thymus gland. The trachea was diverted to the right. The upper lobe of the lung showed a pneumonic infiltration. It is conceivable that the diversion of the trachea to the right may have been due to the negative pressure effect exerted by the consolidated lung on the right side rather than the + 4 enlargement of the thymus gland.

That stridor may be caused by nasal obstruction is illustrated by the following case:—

Case 5.—J. C., male, birth weight 7 pounds, had marked stridor since birth and marked indrawing of tip of sternum and suprasternal notch on inspiration. The clinician who examined the infant diagnosed enlargement of the thymus gland as the cause of the symptoms. The x-ray picture of the chest showed no enlargement of the thymus gland and no compression-stenosis of the trachea. The cardiac silhouette, however, was increased in all its diameters, and the roentgenologist made the diagnosis of congenitally enlarged heart. The stridor persisted until six months of age when relief was afforded the retronasal obstruction by removal of very large adenoids. Very soon after the operation the stridor disappeared.

Of the 322 newborn infants that showed enlargement of the thymus gland on x-ray examination, 276 showed no symptoms; thirty-one showed vomiting; eight suffered from cyanosis; three had vomiting and cyanosis; two had vomiting and dyspnea; two suffered from vomiting, cyanosis, dyspnea, and choking. We feel that simple vomiting in itself should not be considered as a symptom of enlargement of the thymus gland, for that symptom alone occurred with almost equal frequency in the group of infants that showed no enlargement of the thymus gland; in other words, simple vomiting occurred in 9.6 per cent of the babies who showed enlargement of the thymus gland and in 8 per cent of a random group of 100 cases that showed no enlargement. Pylorospasm was diagnosed once in the group of 100 cases that showed no enlargement of the thymus gland. It also occurred once among the 322 cases that showed roentgenologic evidence of thymic enlargement, and that was a baby with a + 4 enlargement. Out of the 322 cases, therefore, only fifteen showed symptoms that might be referred to the thymus gland, making a percentage of 4.7. Of these fifteen infants that showed both so-called "thymic symptoms" and enlargement on x-ray examination; two were of the + 1 type, four of the + 2; five of the + 3; and four of + 4 type. When we consider the entire group of 1,074 babies that was investigated, we see that fifteen out of 1,074 showed symptoms that might be referable to the thymus gland, or 1.4 per cent of all patients showed possible thymic symptoms. In nine of the fifteen patients showing thymic enlargement by x-ray, there was also some other condition that

might have been responsible for the symptoms. The appended list enumerates the nine cases that showed thymic enlargement.

1. Atelectasis of right lung and +2 enlargement. Improved without treatment.
2. Atelectasis of right lung and +2 enlargement. Two x-ray treatments.
3. Atelectasis of left lung and +1 enlargement.
4. Atelectasis of both lungs and +2 enlargement. Treated.
5. Atelectasis of left lung and +2 enlargement. Treated, improved.
6. Atelectasis of right lung and +1 enlargement. No treatment improved.
7. Tracheo-esophageal fistula and +1 enlargement. Death.
8. Cerebral hemorrhage and +2 enlargement. At autopsy thymus was found to be only 1 inch wide and 1 inch long, with practically no depth.

We see thus that out of fifteen cases showing x-ray evidence of enlarged thymus and symptoms, in nine cases there was some other cause than large thymus present. *This reduces to six, or 1.9 per cent, the number of babies in whom the symptoms could not with any degree of certainty be ascribed other than to the enlarged thymus.*

Out of 752 newborn babies that showed no thymic enlargement, thirty-one suffered from dyspnea and cyanosis, or dyspnea, cyanosis, and vomiting. The causes of these symptoms were as follows: twenty-four had atelectasis of the lungs (ten on the left side, eleven on the right side, and three in both lungs); two had cerebral hemorrhages, one cerebral hemorrhage with atelectasis; one pylorospasm; two suffered from cyanosis and dyspnea that could not be accounted for. We see, therefore, that almost an equally large number of babies showed symptoms without x-ray evidence of enlargement of the thymus as those who did show roentgenologic evidence of enlarged thymus; the exact percentage being, in the former, thirty-one cases out of 752, or 4.1 per cent, and in the latter, fifteen cases out of 322, or 4.7 per cent. *Most important is that two babies in 752, or 0.4 per cent, had "thymic symptoms" with negative x-ray findings.*

Eight of the infants in our investigation came to autopsy. Two of them belonged to the group that showed x-ray evidence of enlargement of the thymus gland. One case was a +2 enlargement but at autopsy the thymus gland was found to be unusually small, 1 inch wide and 1 inch long, with practically no depth. The causes of death were cerebral hemorrhage and bronchopneumonia. The other case showed a +1 enlargement, and the autopsy showed a very small thymus gland. The symptoms during life were cyanosis, choking during feeding, regurgitation, and vomiting. The autopsy disclosed esophageal and duodenal occlusion and a tracheo-esophageal fistula. The remaining six cases belonged to the group that showed no enlargement of the thymus gland;

three of them died of cerebral hemorrhage, one of complete atelectasis of the left lung, and two of atelectasis associated with pneumothorax.

Out of 322 cases that showed thymic enlargement, 131 or 41 per cent, received x-ray treatment; ninety-five received one treatment, and thirty-six received two or more treatments. All of the forty-five +4 cases received x-ray treatments; thirty-five received one radiation while ten received two or more treatments. Out of the fifty-one +3 cases, fifty received treatment; in this group thirty-five received one while fifteen received two or more treatments. Out of the seventy-six +2 cases, only twenty-eight were treated, eighteen having received one; and the remaining ten, two or more treatments. Only eight infants were treated out of the 150 +1 cases, of which seven received one radiation while one received two; in other words, 131 infants received x-ray treatment for enlargement of the thymus gland, despite the fact that only fifteen had symptoms customarily referable to an enlarged thymus. As stated elsewhere, in nine out of fifteen infants that showed x-ray evidence of enlarged thymus and so-called "thymic symptoms," there were some other causes than large thymus operable. We see, therefore, that 131 babies were treated, in spite of the fact that only six actually showed symptoms usually referred to the thymus gland and also x-ray evidence of enlargement. We cannot help being forced to the conclusion that a great many of the newborn babies are unnecessarily subjected to a method of treatment, the exact immediate effect of which we do not know and the ultimate results of which are also beyond our sphere of present knowledge. In this connection, the warning given by Morse[28] is timely, namely, that "the demonstration by the roentgen ray of what is assumed to be an enlarged thymus does not prove that such symptoms are connected with it. Even if the symptoms cease after shrinkage of the thymus with the roentgen ray, it does not prove that they were due to a change in the secretion of the thymus. They cease many times without such treatment, and, if the cessation occurs after treatment with the roentgen ray, it may just as well be due to the disappearance of the real and unknown cause." Griffith and Mitchell[29] conclude that "the indiscriminate exposure to the roentgen ray of every newborn baby who supposedly has an abnormally large thymus shadow yet is without clinical symptoms, is a procedure to be deprecated as not only unnecessary, but possibly harmful."

COMMENT

Friedleben's[7] original conclusions, which are based on classic experiments and clinical studies of the thymus gland, could be resurrected with propriety and with a great deal of profit. His dictum, "Es gibt kein asthma thymicum" (There isn't any thymic asthma), is as deserving an observation as that of the fallacy of "laudable pus." While rarely there may be some one or more symptoms such as dyspnea and

stridor due to pressure of the thymus gland, certainly in newborn babies true or actual thymic asthma hardly, if at all, exists. Even the discovery of an enlarged gland in cases of congenital laryngeal stridor does not necessarily prove that pressure from the thymus is the cause of the symptom. Weill-Halle and Dreyfus-See[30] performed thymectomy without sufficient improvement of the stridor to permit the deduction that the enlarged thymus was responsible for the stridor.

There is no question that occasionally one sees a case of marked dyspnea and choking that is actually due to a large compressing thymus which could be demonstrated both anatomically as well as bronchoscopically. Jackson,[31] in his pioneer and classic studies, reported undoubted cases of tracheostenosis which he observed bronchoscopically, in which the narrowing of the tracheal orifice was due to an enlarged thymus, but those cases are rather rare and are not nearly as commonly found as the diagnosis is made. Chevalier Jackson,[31] in a personal communication to the authors, says that a partial review of his records revealed notes of endoscopic findings of thymic compression of the trachea in 127 cases out of 2,182 children examined bronchoscopically for various indications, including foreign body present or suspected. This makes the incidence of 5.8 per cent of thymic compression in Jackson's cases. Of the 127 cases, 114 children had respiratory symptoms (asthmatoid wheeze and stridor); in the others the compression was not sufficient to cause obstructive symptoms. *The diagnosis was made bronchoscopically.* Undoubtedly the majority, if not all, of the patients in Jackson's series were not newborn babies—which is the problem that concerns us—but older children that were brought to him for various disorders associated with the respiratory system, most of them being children who were suspected of, or actually suffered from, foreign bodies in the respiratory or upper alimentary tracts. It is erroneous for most authors to quote Jackson's figures on tracheostenosis due to pressure by an enlarged thymus when referring to the newborn baby. As careful an observer as Finkelstein[4] says that he never saw a case of so-called thymic asthma in which there was actual evidence of compression of the windpipe. He states that the cases which he had earlier diagnosed as thymic and which were confirmed by x-ray examination, on more critical analysis later proved to be due to some other condition. Abt and Helmholtz[32] also doubt the clinical existence of thymic asthma. Even though tracheal compression has been carefully looked for by pathologists, very few have reported positive findings. Marine[1] sums up his review very succinctly. He concludes that "in the great majority of the cases, no clinical or postmortem evidence exists that death is caused by compression and that the explanation of thymic asthma or thymic death is not so simple, or at least that pressure-effects are inadequate in the absence of a constitutional predisposition to account for death." Symmers[33] reports that out of 5,652 autopsies on adults as well as children at the

Bellevue Hospital, status lymphaticus was found in 457 cases, or 8 per cent. The heaviest thymus in that group weighed 70 gm. "But," remarks Symmers, "according to Tammassia, experimentally, the thymus must weigh at least 180 grams before it will compress the trachea."

While we do not want to appear too dogmatic in maintaining that enlargement of the thymus gland does not produce so-called "thymic symptoms," it certainly appears from our study of the literature as well as our own cases, that the etiologic relationship between thymic hypertrophy and the "thymic syndrome" is a very questionable one and that the condition of true tracheostenosis in the newborn, due to enlargement of the thymus, is extremely rare. Griffith and Mitchell[29] say that "a study of the literature together with our own experience appears to us to justify the statement that there is little if any correlation between size of roentgenographic shadow and clinical symptoms which could be attributed to enlargement of this organ." It appears to us that it certainly would seem advisable to divide the cases of so-called "enlarged thymus" into (1) symptomatically enlarged thymus and (2) nonsymptomatically enlarged thymus. The former should only be diagnosed where the symptoms cannot be explained by any of the aforementioned conditions that give the same symptom-complex, and where the x-ray pictures—taken both on inspiration and expiration in the lateral as well as the anteroposterior views—show unmistakable evidence of enlargement of the thymus, particularly if the gland shows a +3 or +4 type of hypertrophy.

SUMMARY

1. Opinions are adduced from the medical literature to show that there apparently exists neither a relationship between so-called "enlarged thymus" of the newborn and sudden "thymic death," nor between the "enlarged thymus" of the newborn and "status lymphaticus."

2. The normal size and weight of the thymus gland are discussed, and emphasis is laid upon the great fluctuations in the weight of the normal thymus and of the variations of the weight of the gland in health and disease.

3. The literature is partially reviewed on the incidence of the diagnosis of "enlarged thymus" as made by x-ray examination. Our investigation includes 1,074 newborn infants, of whom 322 or 30 per cent showed roentgenologic evidence of "enlarged thymus."

4. A roentgenologic classification of enlargement of the thymus gland is offered, in which the +1 type represents the slightest breadth enlargement of the gland, and +4, the most marked width and depth enlargement.

5. Almost 50 per cent of the 322 newborn infants that showed enlargement belonged to the +1 type. The school, therefore, which maintains

that the "thymic syndrome" is caused by pressure would admit elimination of the 150 cases of the +1 type, thus reducing the incidence of roentgenologically enlarged glands to 16 per cent. For the group that claims that the "thymic syndrome" results from increased chemical secretion, the incidence of roentgenologically "enlarged thymus" would have to remain 30 per cent.

6. Of the 322 infants in whom a roentgenologic diagnosis of "enlargement" was made, 150 showed a +1 hypertrophy; seventy-six were +2, fifty-one of the +3 type, and forty-five belonged to the +4 group.

7. Of the 322 babies who showed roentgenogram evidence of "enlargement," 276 showed no clinical symptoms; thirty-one suffered only from vomiting, a symptom that occurred with almost equal frequency in a group of 100 unselected newborn who had no x-ray evidence of "enlarged thymus"; only fifteen of 322 infants, or 4.7 per cent showed symptoms that might be referred to an enlarged thymus gland. Of these fifteen, two belonged to the +1, four to +2, five to +3, and four to +4 type.

8. Of the entire group of 1,074 babies, only fifteen, or 1.4 per cent, showed possible thymic symptoms. In nine of the fifteen infants there was also some other additional condition (atelectasis, cerebral hemorrhage, and in one, tracheo-esophageal fistula) that might have been responsible for the symptoms, thus leaving only six babies or 0.56 per cent in whom the symptoms could with any degree of certainty be ascribed to an enlarged thymus gland only.

9. Of the 322 infants with enlarged shadows, 131 received treatments by x-ray, in spite of the fact that only six actually showed symptoms that might be referable to thymus gland.

10. The suggestion is made that hereafter cases be divided into (1) symptomatically enlarged thymus gland and (2) nonsymptomatically enlarged thymus gland, and that the former be diagnosed only when, in the presence of pressure symptoms, there is unmistakable roentgen evidence of enlargement, particularly if the hypertrophy be of the +3 or +4 type, and when all other conditions elsewhere mentioned have been excluded.

CONCLUSIONS

1. The diagnosis of "enlarged thymus gland" in the newborn is made entirely too frequently and is often based merely on the roentgenologist's findings.

2. True hypertrophy of the thymus gland in the newborn causing tracheostenosis and the typical chain of symptoms is much rarer than it is commonly believed to exist.

3. It is considered inadvisable, unnecessary, and economically inexpedient to examine routinely by x-ray every newborn infant for roentgenographic evidence of enlargement of the thymus gland.

4. There is no indication for x-ray treatment of the thymus gland in the newborn unless the infant shows a symptom, or chain of symptoms, pointing to hypertrophy of the thymus gland, and for which symptom the clinician has carefully excluded other causes, and wherein the roentgenologist has demonstrated unmistakable evidence of depth enlargement.

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BULBAR POLIOMYELITIS AND ITS TREATMENT

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OUR purpose in writing this paper is to present a clinical picture of the more common types of bulbar poliomyelitis; to outline the criteria for determining the prognosis of a given case; and to discuss the therapeutic measures which have been advocated and those which we have employed in the treatment of our patients and in the prevention of complications.

Our experience with the poliomyelitis epidemics of 1931 and 1933 shows that the following are the common types of acute anterior bulbar poliomyelitis.

1. *Unilateral Paralysis of the Palate.*—Following the acute prodromal symptoms of headache, vomiting and fever, the patients complain of pharyngeal discomfort for one or more days and then present the following clinical picture. The palate, posterior pharyngeal wall, fauces, buccal mucous membranes, and gums are uniformally congested. The tongue is coated white, and the papillae project. One-half of the palate lags behind and the healthy side alone pulls upward; hence the median raphe and uvula deviate to the sound side when the patient utters a long "ah." A small amount of mucus is seen stagnating on the paralyzed side. The voice is occasionally slightly nasal, and swallowing is difficult for one or two days only. Very frequently the power of coughing is much diminished owing to the inability to bring the vocal cords firmly together. One-half of the tongue may be involved; the paralyzed half of the tongue feels to the patient as if he had a foreign body in the mouth. When the tongue is protruded, the healthy side causes the tip to be pushed round to the paralyzed side in a sickle-shaped curve. The patients are generally neither drowsy nor restless. The temperature gradually subsides within from five to ten days, and then recovery ensues. Forty-nine per cent of the bulbar cases seen by us were of the unilateral type.

2. *Bilateral Paralysis of the Palate.*—The patients in this group, like those described above, show the same prodromal symptoms. With the onset of bulbar poliomyelitis, the clinical picture assumes its characteristic features. The patient becomes nauseated and salivation increases. All parts of the oral cavity are evenly congested. Mucus collects behind the posterior pillars and, when abundant, covers the entire posterior

From the services of Drs. Harold L. Barnes and Benjamin Kramer, Kingston Avenue Hospital for Contagious Diseases.

pharyngeal wall. The uvula is seen submerged in the saliva. The cough is weak, and, although the patients are able to bring the mucus to the pharyngeal space, they are unable to expectorate. Respirations are somewhat labored, but there are no supra- or infrasternal retractions. As the column of air passes through the pool of mucus during expiration, it produces a gurgling sound. The soft palate hangs like an apron and does not move on articulation. The nasal cavity therefore cannot be shut off from the mouth. As a result the voice is nasal, and certain consonants are altered ("b" becomes "m"; "d" becomes "n," etc.) so that articulation as a whole is indistinct. This indistinctness of articulation is increased when the patient stoops forward; it diminishes or even disappears on his lying with the head thrown backward, since in the latter position the paralyzed soft palate tends to fall back by its own weight and shuts off the nasopharynx. Swallowing is difficult or impossible, especially of liquids which, during the act of deglutition, regurgitate into the nasopharynx and escape through the anterior nares. Epigastric pain is a frequent complaint. The temperature is the only prognostic sign as to the spread of the infection. As long as the temperature remains elevated, the infection is liable to spread to some other part of the bulb and cord. We have never seen paralysis extend after the temperature has remained normal for forty-eight hours. Recovery in these cases is very slow and the signs and symptoms may persist for many weeks. Complete palatine paralysis comprised 51 per cent of the total number of bulbar cases.

The patients described* do well and eventually recover completely. The following patients, however, do not present as favorable a prognosis and are the cause of utmost concern to the physician.

When, in addition to the signs and symptoms of the two types described above, parts of the vagi which supply the cardiac, respiratory and gastrointestinal systems are affected, the following result: gastric dilatation with vomiting and pain; loss of the oculocardiac reflex; tachycardia and irregularity of the heart (due to paralysis of the cardiac inhibitory fibers); and slowness and irregularity of respirations. Drowsiness or extreme irritability and restlessness may also be noted.

If the damage to the vagal nuclei is minimal and transient due to edema, we may hope for a disappearance of the above dangerous signs and symptoms within a short period, with ultimate recovery. However, when there is more or less permanent involvement of the affected parts due to hemorrhage or destruction in the bulb, the outlook is grave. The vomiting continues at intervals; the epigastric pain persists; restlessness increases; the quality of the heart action becomes poorer, the tachycardia and irregularity becoming more marked; and a fatal termination

*We have not discussed facial paralysis in these groups because the nucleus of the seventh nerve is in the pons and we are describing only bulbar paralysis.

is the result. It is therefore apparent that the gravity of the involvement of the vagi will depend upon the extent and type of the lesion in their nuclei.

The type of bulbar poliomyelitis which, in our experience, has proved to be invariably fatal, is the one in which there is involvement of the vasomotor center. Here, in addition to the picture of vagal damage, the patient presents the syndrome of extreme vasomotor collapse; the pulse is rapid, weak, thready, and of low tension; the respirations are shallow and irregular; the muscles are relaxed; there is mental apathy; the face is expressionless; the skin is cyanotic, cold and clammy; the pupils are dilated; the temperature gradually rises, and the blood pressure falls. Death is the inevitable outcome. The mortality rate in our series of cases was 25 per cent.

TREATMENT

Lumbar Puncture.—The consensus of opinion of previous investigators is that lumbar puncture is of therapeutic value in the treatment of all types of poliomyelitis.[1] Our experience with 1,325 cases, of which 29 per cent were bulbar, causes us to feel that lumbar puncture is unnecessary and definitely contraindicated in bulbar poliomyelitis in which paralysis is self-evident. Where the diagnosis is doubtful and a lumbar puncture is essential, a small amount of fluid should be slowly withdrawn.

A brief review of the histology and physiology of inflammation will clearly indicate the reasons for our belief. The capillaries in the affected areas are dilated and injected with acceleration of the blood stream. Soon hemostasis with engorgement and tortuosity of vessels occurs, followed by exudation into the affected part. Occasionally petechiae are also present. The object of the exudation is twofold, to bring antibodies to the inflamed area and to support the capillary walls and prevent their rupture. The pressure of the exuded fluid in the cord proper is therefore equal to the spinal fluid pressure in the subarachnoid space, and the capillary walls are consequently held intact. When the subarachnoid pressure is suddenly released by lumbar puncture the pressure within the cord is similarly released. The spinal cord instantly bulges; the capillaries dilate and blood rushes into them. With the sudden onrush of blood, oozing takes place from the finer blood vessels, and additional capillary ruptures in the bulb are liable to occur and in many instances probably do occur. When the bulb is the site of hemorrhage, enormous edema results; the vital centers are strangulated; and death is sure to follow.

Furthermore, it is claimed by previous investigators in this field that repeated lumbar puncture diminishes intracranial pressure; and headache, vomiting, and hyperesthesia disappear. It is common knowledge among clinicians that children suffering from acute poliomyelitis rarely

vomit more than once and that the headache subsides in one or two days with or without lumbar puncture. These two symptoms cannot, therefore, be attributed to persistent increased intracranial pressure since they subside so rapidly. In the light of present knowledge of the pathology of poliomyelitis, one is inclined to attribute the hyperesthesia to posterior root infiltration, a constant microscopic finding, rather than to increased intracranial pressure. The hyperesthesia lasts for a long time after the increased intracranial pressure has subsided. We must conclude that repeated lumbar puncture does not benefit the patient, and on the contrary, subjects him to the danger of hemorrhage into the bulb.

Respirator.—The use of the respirator is definitely contraindicated in these cases. The respirator is indicated in intercostal, diaphragmatic, and abdominal muscle paralysis, in which prolonged artificial respiration is required. No such paralysis is present in pure bulbar poliomyelitis. Paralysis of the respiratory center, when and if it occurs, is part of the vasomotor collapse and a phase of the terminal picture.

Drugs.—All drugs that depress the respiratory center are definitely dangerous and contraindicated. Atropine sulphate has been advocated and used extensively for the purpose of drying up the secretions in these cases. It must not be overlooked that when given in larger doses atropine sulphate is a depressant of the respiratory center. Therefore we believe that its repeated use is inadvisable.

Postural drainage and suction.—Patients who are unable to swallow, either because of partial or complete palatine paralysis, are treated in the following manner:

Upon admission to the hospital and immediately following physical examination, the child is put to bed in a prone position upon a hard mattress. The ankles are well padded with cotton and tied by means of a bandage to the foot of the bed which is elevated about two feet so that the head is well down. If the child is restless and insists upon turning, the wrists are attached to the sides of the bed. This posture is maintained to insure drainage.[2]

Usually there is a marked flow of mucus from the mouth and nose. Frequently, however, though most of the secretions are removed in this manner, a considerable amount of the mucus may remain in the pharyngeal space and stagnate behind the posterior pillars. In this event there is danger of aspiration pneumonia and the development of catarrhal or purulent otitis media. To diminish the possibility of these complications, suction is instituted by gently introducing a suction catheter into the mouth and throat. The patient usually resents this form of treatment for the first two or three times, but he thereafter becomes accustomed to this procedure and willingly submits to it and, in fact, very often begs for it.

Feeding.—Since swallowing is impossible and nausea is present, three or four ounces of tap water, at body temperature, are introduced per rectum every four hours by means of a funnel and catheter during the first day. On the next day, in addition to tap water by rectum, hypodermoclyses of 5 per cent glucose in normal saline are started. The use of hypodermoclysis is delayed in order to prevent excessive restlessness during the child's first twenty-four hours in the hospital. Two daily hypodermoclyses and instillations of water by rectum are continued as long as nausea persists. We have found that the restlessness and nausea correspond to the period of temperature.

Nasal gavage is not begun until the temperature has subsided. Regardless of the age of the patient, the amount of fluid in the first gavage should not exceed two ounces, for the child frequently vomits the first food introduced in this manner. The amounts are gradually increased until a maximum of 8 ounces every four hours is reached. This is usually established at the end of twenty-four hours. Henceforth the child takes his nasal gavage without difficulty. The gavage diet given every four hours consists of the following ingredients:

Milk	8 ounces	160 calories
Sugar	2 ounces	240 calories
One egg		80 calories
		480 calories

Children with one-half of the palate paralyzed are usually able to swallow at the end of forty-eight hours. In those with involvement of both sides of the palate, the inability to swallow may be prolonged for as long as six or seven weeks. As soon as the palate begins to move, the patient is placed in a supine position without a pillow, and a semisolid diet is given. The head is then slowly elevated from day to day until the child is able to take nourishment without any difficulty. All these precautions are observed in order to decrease the possibility of the occurrence of aspiration pneumonia.

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CONGENITAL HEART DISEASE

Pulmonary Stenosis of Inflammatory and Developmental Origin Complicated by Rheumatic Heart Disease and Subacute Bacterial Endocarditis

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THE most frequent type of congenital heart disease found with the symptom-complex of so-called congenital cyanosis is a stenosis of the pulmonary artery with its associated cardiac defects (Abbott[1]). In a statistical analysis of one thousand cases of congenital heart disease made by Abbott,[2] stenosis of the pulmonary artery was found in 110 cases.

The cases of pulmonary stenosis have been divided by Abbott[1] into two groups: first, those in which the "lesion is purely valvular and has resulted from endocarditis of the pulmonary segments setting in during relatively late fetal life after the cardiac septa have closed"; and second, "the other and much larger group of pulmonary stenosis where the lesion is to be traced to an arrest of development in early embryonic life before the division of the heart into its four chambers is completed." In the former group of cases "which are considered here first, as the less complex anomaly, there is a thickening and usually a fusion of the pulmonary cusps with the production of a small, often funnel-shaped, pulmonary orifice, which opens off the hypertrophied, but otherwise normal, conus of the right ventricle, and the pulmonary artery is usually of normal size or may even be dilated; the interventricular septum is entire, but the foramen ovale is usually patent and is not infrequently fenestrated."

In the latter group, "the main lesion is not inflammatory or valvular, but a true hypoplasia of the pulmonary tract, and the interventricular septum presents a defect at the base; while the aorta, which it will be remembered arises in early embryonic life from the right side of the common ventricle, usually appears displaced to the right, arising from both ventricles above the septal defect or entirely from the right ventricle; the pulmonary artery is usually small and thin-walled and the pulmonary valve bicuspid or rudimentary. The conus of the right ventricle is narrowed, or it may (in cases where a septal defect communicates with the conus) be expanded below the cusps into a chamber connected with the sinus of the ventricle by a constricted orifice (persistent lower bulbar orifice)."

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At times the stenosis is only transient and the congenital lesion may be progressive leading eventually to an atresia of the pulmonary artery. The aorta then dilates. The pulmonary circulation is usually maintained through a widely patent ductus arteriosus or through branches directly from the aorta (Kugel.[3]) This condition has been described as *truncus solitarius aorticus.*

This case is reported because the clinical and pathologic observations may add to our knowledge of this type of heart disease. The pulmonary stenosis is of the relatively rare type belonging to the group of inflammatory origin superimposed upon a true arrest of development, as evidenced by the presence of a patent intraventricular septum, dextroposition of the aorta and some stenosis of the pulmonary conus (tetralogy of Fallot). Of great interest pathologically is the finding of old, mild, healed lesions of all the heart valves (probably rheumatic) with a superimposed, subacute, bacterial endocarditis, while clinically there was an intense polycythemia with its accompanying vascular changes in the eyegrounds and nail beds.

CASE REPORT

J. E., a Porto Rican girl, aged twelve years, was admitted to the Mount Sinai Hospital on November 4, 1932. The family history was entirely negative. Her birth history was normal, and there was no cyanosis at the time. She had pertussis at two and one-half years and measles at ten years of age. During the past nine years, she had had attacks of transient arthralgia in the knees. There was no swelling, redness, or fever. For the past four years she had had frequent severe frontal headaches and nosebleeds. Her menses began when she was eleven years old and have been regular, the periods lasting three to five days. Her first symptoms were noted at two years of age when she developed cyanosis. Her mother stated that she thought the finger nails and toe nails were abnormally curved shortly after birth. Cyanosis was first observed in the lips and nails. It gradually became more progressive, being aggravated by excitement, exertion, or cold. It increased as the child grew older. She complained also of chilly sensations, particularly in her extremities. She was, however, able to play with other children and go to school until she was ten years old when she began to be dyspneic on exertion. This grew progressively more marked, so that at the time of admission she was severely dyspneic and orthopneic. For one year previous to admission she had complained of inability to see clearly, particularly after exertion. Occasionally she had precordial pains. There was no edema, fever, or abdominal pains at any time.

The examination on admission showed an acutely ill child with extreme cyanosis of the lips, face, nose, ears, and extremities. The respirations were rapid, labored, and without pause. The patient was very irritable and in great distress. She complained of inability to see. The temperature was 100° F.; the pulse 156, regular and of fair quality; the respirations were forty per minute. The skin had a generalized dusky hue and was cold and dry. A number of old purpuric spots were seen over the chest and lower extremities. There was marked clubbing of the fingers and toes. The eyes were inflamed; the pupils were round and regular and reacted to light and accommodation; the sclerae and conjunctivae were cyanotic and congested. The ears were normal except for a bluish discoloration of the drums. The nose and throat were negative. The lymphatics were normal. An examination of the chest

showed the heart to be markedly enlarged to the left, and somewhat enlarged to the right. The rate was rapid and the rhythm regular. A rough systolic murmur was heard over the apex, but more distinctly at the third interspace just to the left of the sternum. The second pulmonic sound was muffled. The lungs were clear. The abdomen was soft and the liver was felt about one and one-half fingerbreadths from the costal margin. The spleen was not palpable.

Laboratory Examinations.—The blood pressure was 112/90.

The examination of the eyegrounds (Dr. Minsky) showed the following changes: right eye: the nerve head was crimson in color. The nasal half of the nerve was elevated by the dilatation of the veins and arteries while the nasal margin was indistinct. The arteries and veins were markedly tortuous and glistening. The caliber of the vessels was larger than usual, the branches not ordinarily seen, especially in the macula, being affected. The background had a delicate lavender tint with a crimson base. In the periphery, the vessels were larger than usual.

Left eye: the nerve head was similar to the right. The vessels appeared more turgid, and the veins were markedly dilated. The periphery and macula were similar to that described in the right side (Fig. 1).

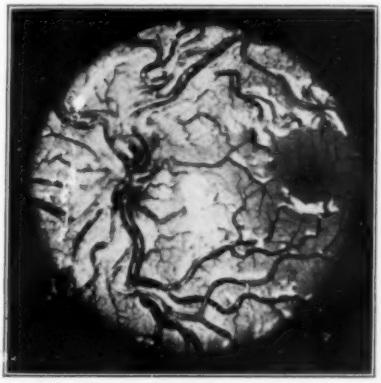

Fig. 1.—Photograph of retina made and lent by Robert K. Lambert showing vascular changes.

A microscopic examination of the capillaries of the nail beds (Dr. Leader) showed them to be markedly increased in size. The vessels were greatly lengthened and widened. They were distended with corpuscles moving at an extremely slow rate so that in many loops an absolute stasis was evident. The vessels were also very tortuous and the normal looped contour was entirely distorted. The arterial and venous limbs were approximately the same size. The vessels were not increased in number. There was no evidence of a subpapillary plexus. The background had a purplish, livid hue. The configuration of the vessels was that usually seen in congenital heart disease with polycythemia and advanced clubbing (Fig. 2).

The blood count showed a hemoglobin content of 138 per cent, a red blood count of 10,360,000, and a white blood count of 4,600. The polymorphonuclear neutrophils were 70 per cent; the lymphocytes, 22 per cent; and the monocytes, 8 per cent. The sedimentation time was over two hours (normal). A urine examination showed a heavy trace of albumin. The blood Wassermann was negative. A blood culture taken shortly after admission was negative. Repeated electrocardiographic examinations (Dr. Hubert Mann) showed high voltage in the main deflection. There was evidence of marked right ventricular preponderance. The P waves were prominent in Leads

I and II; the T wave was prominent and upright in the first lead and sharply inverted in Lead III. The rate was about 130 per minute.

An x-ray examination of the chest showed no abnormality in the lungs. The cardiac shadow was markedly enlarged to the left. The right side showed only a moderate enlargement. The aortic knob was present although it was small. The pulmonary artery pulsation was not visualized, and the second (pulmonary) arc was not prominent or enlarged (fluoroscopic examination). The heart's apex was turned upward on the left in the typical *coeur-en-sabot* configuration. (Fig. 3.)

Course.—Under rest and sedatives, the child improved temporarily. The respirations then became slower and the pulse rate decreased slightly to 120. However, she ran a slight fever daily. About ten days after admission the temperature rose to 102° F. and remained at that level. On the fifteenth day in the Hospital, a number of petechial spots appeared on the chest and abdomen. The blood culture at this time was negative. Nevertheless, the presence of a bacterial endocarditis was suspected clinically. The following day she had a severe attack of cyanosis and died.

Fig. 2.—Drawing of capillaries of nail beds as seen under microscope.

Postmortem Examination.—(Drs. P. Klemperer, L. Lichtenstein, and S. Siegal.) The body was that of a well-developed, well-nourished girl of twelve years, in incomplete rigor mortis. The skin was distinctly cyanotic all over. The conjunctivae, palpebral and ocular, were markedly injected and cyanotic. The nails of the fingers and toes were clubbed and blue. There were a few scattered small, rather faint, petechial spots without white centers upon the anterior chest. Prominent dilated veins were noted especially upon the anterior chest wall, but also upon the abdomen and lower extremities. There was no jaundice or edema present. The blood which escaped from the veins was very dark blue and viscid. The jugular veins were engorged.

The abdomen was not distended. The veins of the mesentery and gastrointestinal tract were engorged. The viscera were cyanotic, enlarged, and greatly congested.

Heart: The heart was greatly enlarged and had a globular shape. The enlargement was chiefly that of the right ventricle. From a view in situ the left ventricle represented about one-quarter of the anterior surface of the heart. This was due to the fact that the left ventricle was much smaller than the right and was displaced posteriorly (Fig. 3). The right auricle received, in its normal fashion, the

inferior and superior venae cavae. The right auricle was somewhat enlarged; its wall was thickened. The mouth of the cornary sinus was widely gaping. The tricuspid valve presented a diffuse thickening throughout, with numerous blood vessels going to the line of closure where there were large, irregular, warty vegetations, which were hard and firm and which showed, on smear and culture, gram-positive

Fig. 3.—Roentgenogram of chest and postmortem specimen of heart as seen in situ.

cocci in pairs (Fig. 4). The chordae tendineae were only slightly thickened. The right ventricle was dilated, and its wall greatly hypertrophied. The thickness of the right ventricle was 13 mm., and there was a marked hypertrophy of the papillary muscles and a great prominence of the trabeculae carneae. The right outflow tract was much thicker than the inflow tract, and the region of the base of the

pulmonary conus presented the greatest hypertrophy of the heart. There was a gaping defect which admitted the index finger in the interventricular septum, near the base of the aorta. The aorta overrode both ventricles. As one followed the right outflow tract upward, one could observe a gradual constriction of the pulmonary conus producing a stenosis at the base of the pulmonary artery. In addition, there was a fusion of the three pulmonary valve leaflets forming a cone with the apex pointing upward and projecting into the pulmonary artery. At the apex of this cone there was a small opening through which blood was forced into the pulmonary artery. There were a few vegetations at the apex of this cone (Fig. 4). The pulmonary artery was of normal size above this area. Its walls, however, were very thin, and the vessel in its entirety was collapsed. The course of the pulmonary artery from this point on was normal. There was no opening found between the pulmonary artery and the aorta. The left side of the heart was smaller than the right. The left

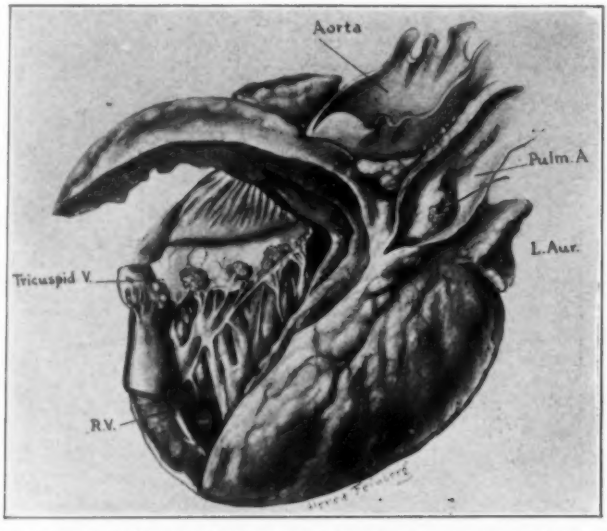

Fig. 4.—Drawing of the right side of heart showing hypertrophy of the right ventricle (R. V.) large growths of vegetation on the tricuspid valve, and probe passing through pinhole stenosis of pulmonary valve.

auricle was of normal size. Its endocardium was only slightly thickened. The foramen ovale was still patent, allowing a coarse probe to pass through it. The mitral valve was diffusely thickened throughout and very well vascularized. Along the line of closure one could see small, shaggy bits of vegetations, which were very flat and minute. Crushings of this vegetation showed gram-positive diplococci. The chordae tendineae were not thickened. The left ventricular wall showed only slight hypertrophy, its thickness being 9 mm. There was a dilatation of this chamber. A septal defect at the base of the aorta allowed free communication with the right ventricle (Fig. 5). The cavity was globular in shape with a slight bulge at the apex. The interventricular septum bulged from the right side into the left, thereby diminishing the size of this cavity. The aorta took its usual origin from the left side and overrode the right only slightly. There were three cusps with blood vessels at the base of each with vegetations on all three valves. There was

a small irregular growth of vegetation on the aorta. The two coronary arteries had their normal origin and distribution. The aorta showed a small depression, which apparently was the ductus arteriosus, and one could follow this inward for about ½ cm. where it was completely closed. Apparently this aperture was not stenosed until later life. The bronchial arteries had prominent mouths and were large.

Diagnosis.—Congenital defect of interventricular septum at base with dextroposition of aorta, and conus stenosis of right ventricle and valvular stenosis (possibly inflammatory) at pulmonary orifice.

Hypertrophy of right ventricle. Patent foramen ovale. Closed ductus arteriosus. Enlarged bronchial arteries. Chronic valvular disease (rheumatic) of the mitral, aortic, tricuspid and pulmonary arteries with

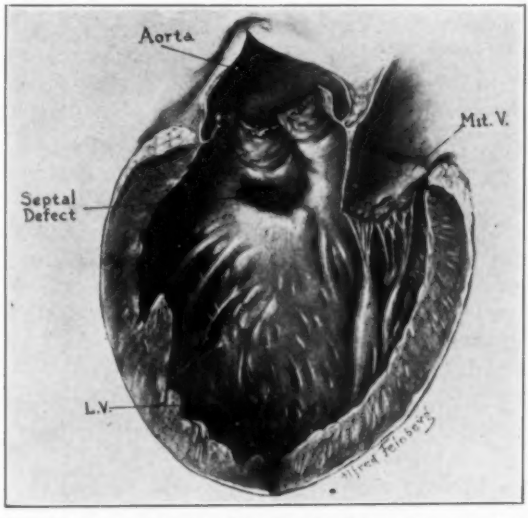

Fig. 5.—Drawing of left ventricle showing septal defect and vascularization of mitral and aortic valves.

vascularization of the mitral, aortic and tricuspid valves. Subacute bacterial endocarditis of all valves. Polycythemia. Congestion of viscera.

DISCUSSION

We have presented the clinical and pathologic findings of a thoroughly investigated case of congenital heart disease which is not only of interest in itself, but is important for later work in this field. Not only are we dealing in this instance with the mechanical defect causing cyanosis, but also with the well-known fact, as emphasized by Abbott,[4] Libman,[5] Wilson,[6] and others, that these individuals are subject to the development of a bacterial endocarditis and rheumatic heart disease. Wilson,[6] in an analysis of five hundred cases of heart disease in children, found

that fifty-six, or 11.2 per cent of these children, were patients with congenital heart defects. "Eighteen, or 3.6 per cent of these, also gave a complicating rheumatic history."

The occurrence of a subacute bacterial endocarditis engrafted upon a bicuspid aortic valve has become a well-known clinical fact due to the work of Abbott[7] and Lewis and Grant.[8] In one thousand cases of the various types of congenital cardiac defects analyzed[2] subacute bacterial endocarditis with endarteritis was present in seventy-three, an incidence of 7.3 per cent, occurring most frequently in cases of patent ductus arteriosus and defects of the interventricular septum. In 110 cases of pulmonary stenosis reported, bacterial endocarditis or endarteritis was found in five cases, an incidence of 4.5 per cent. Rost and Fischer[12] and Fischer[13] found congenital cardiac disease to be present in six of seventy-eight cases of subacute bacterial endocarditis in children whom they either followed or whose cases they collected from the literature, an incidence of 7.7 per cent. Many of the clinical features in these cases are in common with those reported by Abbott[1] and by Rösler.[9] Only the more important ones will be summarized.

Of great interest were the *intra-vitam* studies made of the vessels in the eyegrounds and in the skin. The changes in the eyes as pointed out by Ginsburg[10] are in reality due to the presence of a polycythemia. The severity of the lesions, according to this author, is directly proportional to the degree of polycythemia. He reported three cases in which the red blood counts were 6,500,000; 7,600,000; and 9,800,000, respectively. In the last of his cases, histologic examinations were made which greatly clarified the pathologic background of the retinal picture which one sees *intra vitam*. There was marked thickening and hyalinization of the walls of the dilated vessels in the iris, choroid, ciliary body, and retina. In the left eye a large hemorrhagic infarct was present in the periphery of the retina. In the right eye many vessels showed also endothelial proliferation with narrowing and frequently obliteration of the lumen. Numerous hemorrhages were present between the retina and choroid and in the vitreous humor. Our ophthalmoscopic findings are similar to those described by Ginsburg.[10] In our case the polycythemia was quite marked, the red blood count being 10,360,000 and the hemoglobin content, 138 per cent.

The capillary microscopy of the vessels of the nail beds showed these to be markedly enlarged, tortuous, and distended with corpuscles which were moving very slowly. This picture is typical of that seen in cases of congenital heart disease with clubbing of the fingers and polycythemia (Leader[11]). Similar observations have been made by Redisch and reported by Rösler.

The x-ray findings are of interest, inasmuch as a thorough fluoroscopic examination was also made. From the teleroentgenogram the enlargement seemed to be due to the left ventricle. However, a knowledge of

the pathology of this condition from previously reported cases, as well as the bulging of the right auricular contour, indicated that the changes in the right ventricle were greatly responsible for the enlargement and contour of the heart. This was further corroborated by the electrocardiographic findings which are usually associated with a right ventricular preponderance. The lack of pulsation and bulging of the pulmonary artery is explained by the stenosis of the conus, the pinhole opening of the pulmonary valve, and the collapse of this vessel. Fig. 3 shows a photograph of the heart attached to the lung, in a position similar to that found in life in an attempt to correlate the teleroentgenogram with the position of that organ during life.

It is evident from an analysis of the pathologic specimen that we are dealing with a case of congenital cardiac defect due to a congenital maldevelopment of the pulmonary artery and a secondary inflammatory stenosis of the pulmonary valves. The patency of the interventricular septum points to the conception of a primary congenital defect. The stenosis of the pulmonary valve may have been due either to a nonspecific infection or to rheumatic fever. It is interesting to note that since the age of three years the child has had frequent attacks of pains in the joints, which pain may have been manifestations of recurrent attacks of acute rheumatic fever. The subacute bacterial endocarditis complicated this picture and hastened the inevitable end.

SUMMARY

A case of congenital conus stenosis of the right ventricle complicated by a valvular stenosis of inflammatory origin with fusion of the pulmonary cusps forming a pinhole orifice has been described. It was further complicated by the presence of a healed rheumatic endocarditis and a fresh subacute bacterial endocarditis.

Complete pertinent clinical and laboratory data have been presented.

We wish to acknowledge our appreciation to Doctor Bela Schick, Doctor Maude Abbott and Doctor Louis Gross for their helpful review of this case.

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MALADAPTATION AS A FACTOR IN THE ETIOLOGY OF NEUROSIS

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THE definition of health is one that is not easy to give although in general it is fairly readily understood. It is a truism that the normal is a wide and varying standard and that the pathologic shades into the physiologic by imperceptible degrees. And yet broadly, the concepts of health can clearly be formulated. From the biologic standpoint, health means simply a more or less perfect adaptation to environment. We say an organism is adapted when its reactions to the external world are favorable to the continuance of physiologic functioning.

But adaptation must be made on the mental as well as on the physical plane for the soundness of mind and body. It is not a new theory that psychopathologists are holding out, that poor psychic adaptation is at the bottom of much of the neurosis we see, yet it is only recently that as much attention has been given to this phase of the subject as it has deserved.

The relation of body and mind is a problem as old as philosophy and perhaps as unsettled as ever, but that some relation exists every one knows. Mental pain or suffering, we are aware, if prolonged in any form makes its inroads on the body. The overwrought man failing in business eventually breaks under the strain of his worry: the grief-stricken one, who cannot reconcile himself to the loss of a relative, declines in health; the woman with a strong instinct for maternity often becomes a physical sufferer if deprived of motherhood; the surgeon, too, knows how much the chances for shock are increased in a patient who frets much about the approaching operation. In certain instances of intense or sudden emotional shock, death may result.

These phenomena are merely common observations in the daily life of us all, and they illustrate that a mind not at ease has within it power to produce physical suffering. We know that in most neurotics a constant anxiety is always with them, and they never attain the equipoise of the normal individual. It is a perpetual problem with them to adjust themselves to reality; as a result we see them going about entirely out of harmony with their surroundings. In short, there is always some conflict within their psychic sphere, always some mental pain in the form of phobias, obsessions, anxieties, hatreds, jealousies, feelings of inferi-

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ority or self-insufficiency, that stamps them as being very abnormal temperamentally. In fact, a study of these people convinces us that we are dealing more with anomalies in emotions and personalities than any other thing. They are persons who have made a failure in their adaptation to the conditions of civilized life and consequently break down under the excessive strain. The amount of stress and strain thrown on an individual to bear is largely determined by his temperament—that is, by his attitudes toward life, his reactions toward situations, and the manner of meeting problems before him. To those whose temperaments have become stabilized, living becomes relatively easy with a minimum of nervous strain, but for those who have never reached this solidity, accommodation to even ordinary conditions of life is difficult and accompanied by much wear and tear on the nervous system.

The effect of maladaptation and psychic conflict upon the health of the individual was well shown by those suffering from "shell shock" in the late war, for it is pretty well agreed now that war neuroses were psychic in origin and arose from the inability of the soldier to adjust himself to the strenuous conditions of war. It was just those soldiers, too, who were unable to fit easily in civilian life who broke first in the trenches though many of them had passed perfect physical examinations, and the nervous disturbances they suffered were in no way different from those of peace time. Sir James Purves Stewart, whose experience with shell shocked soldiers was very large, says: "There is no exclusive war neurosis." That is, there is no neurosis in war which we do not see in civil life. Furthermore war neuroses are not confined to the combatants; they occur during war times in peaceful citizens, not only in those exposed to incidents of war such as aerial raids and other bombardments, but even in individuals far removed from such experiences, that is, among home relatives and friends of soldiers or in timorous conscripts who have never been anywhere near the fighting line.

If it be true that these unfortunate misfits are suffering with temperamental incompatibilities with environment, the prophylaxis and treatment depends upon either changing the temperament or the environment. In children, with whom this paper is largely concerned, this will be much easier than in adults. Doubtless the nervous temperament is to a certain extent inherited but surely not as much as we formerly believed. It is, perhaps, not so much the nervousness that is inherited as it is a sensitive nervous structure that reacts more intensely to situations than is normal. Biologists are giving more and more attention to the molding effects of environment rather than to the formerly overstressed importance of heredity. Innate mechanisms plus the working of environment are what eventually determine the character of any organism; but in estimating the influence of heredity, we have usually been blinded by the early effects of environment. It is well known that man is very impressionable to his surroundings in his early years as

compared to his later ones, and the saying, "You can't teach an old dog new tricks," is figuratively true. When adult life is reached, temperament is largely fixed and changes slowly under any conditions. In early life it is different. In the words of Cameron, the young child is merely a mirror of his environment and reflects back every influence brought upon him. In his masterful essay on habit, William James says:

"There is no part of the organism in which the reconstructive activity is so great during the whole period of life as it is in the ganglionic substance of the brain, and this nervous structure is peculiarly liable to modification during the early period of life in which the functional activity of the nervous system, and particularly the brain, is extraordinarily great and reconstructive processes proportionately active."

What is so clearly true of the nervous apparatus of animal life can scarcely be otherwise than true of that which administers to the automatic activity of the mind. The psychical principles of association, indeed, and the physiologic principles of nutrition simply express the universally admitted fact that any sequence of mental action which has been frequently repeated tends to perpetuate itself so that we find ourselves automatically prompted to think, feel, or do what we have been before accustomed to think, feel, or do under like circumstances without any consciously formed purpose or anticipation of results. The strength of early association is a fact so universally recognized that the expression of it has become proverbial.

In accordance with these principles then, it is but logical that the child will grow up exhibiting the same characteristics as parents with whom he was almost exclusively associated in the most impressionable years of his life. For up until the school age, little influence outside the home is ever encountered, and by that time the character and temperament has already taken a strong set, forming attitudes that will direct it through life. To use an old simile, the tender plant just emerging from the earth, may take only a slightly perceptible change of direction by impinging against the clod, but the new set determines the direction in which it will grow in mature life when it has become a tree. The influence of the clod is strongly seen. So in childhood, the early home environment determines the mold to which one grows and can never be wholly effaced.

In neurotic children it is the rule to see the same tendencies in one or both parents and the effect of almost constant and exclusive association in this nervous environment at the time of life when temperament is taking its irrevocable set, is one that is lasting throughout life. On this subject the late J. J. Putman, formerly Professor of Nervous Diseases at Harvard, has this to say: "When parents and child exhibit the same symptoms, it can often be shown to have been the influence of the nervous ignorant mother driven by a fatal impulse to strive

toward reproducing herself in the child and the fatalistic impulse of the child to imitate the mother, rather than any hereditary tendency that brought the result to pass."

Thus it is, the environment in the home makes for habits of anxiety and irritability or for mental rest and quietude and so determines much the present and future health of the individual. In his volume on the nervous child Cameron says: "The body of the child is molded and shaped by the environment in which it grows. It is the outstanding rapidity, which the mental processes develop, that forms the distinguishing characteristic of the infancy of man. Were it not for this rapid growth of the cerebral functions, the rearing of children would be a matter almost as simple and uneventful as the rearing of livestock; for most animal faults of environment must be very pronounced to do harm by producing mental unrest and irritability. Thus indeed some wild animal separated from its fellows and kept in captivity may sicken and waste, though maintained and fed with every care. Yet if the whole conditions of life for the animal are not profoundly altered, if the environment is natural or approximately natural, it is, as a rule, only necessary to care for its physical needs, and we need not fear that the result will be spoiled by the effects of the mind on the body. With the child it is different; airy nurseries, big gardens, visits to the seaside, and every advantage that money can buy, will not achieve success if the child's mind is not at rest, if his sleep is broken, if his food is habitually refused or vomited, or if to leave him alone in the nursery a moment is to evoke a fit of passionate crying."

In children, as in adults, nervous symptoms may be prominent although the physical surroundings of the patient may be all that could be desired. The unstable mind of the child is so sensitive that cerebral fatigue and irritability are produced by causes that seem extraordinarily trivial. In the simple life which a young child leads, it is not always easy to perceive just where the cause of nervous overstrain may lie. But it is usually in the personality of the mother or nurse, in her conduct toward the child, in the tone of her voice, in her very word or action. The mental environment is created by the mother. There are many women who, without any deep thought on the matter, have the inborn knack of managing children; they seem to understand them, and we say the children are always good in their keeping. But then there are others who are indeed lacking in this respect; in their care, children are quickly demoralized, sleeplessness, irritability, fretfulness, anorexia, and a host of other ills soon make their appearance.

It is through the enormous susceptibility to suggestion that a great part of the educational and temperamental development of the child transpires. In its essence, the problem of managing children has largely to do with the regulation of the interplay between the adult mind and that of the receptive suggestible child. Nervous and apprehensive

parents, who are distressed when the child refuses to eat or sleep and who worry all day over possible sources of danger, are forced to watch their child acquire a reputation for nervousness which, as always, is passively accepted and consistently acted up to. As just pointed out, the disturbing and irritating element in the young child's environment is the artless intrusion of the adult mind. With an only child it is difficult to avoid this fault. His existence consists entirely of the preoccupations of his parents with his welfare. He rapidly grows incapable of living without this stimulation and the constant society and attention of adults. He cannot be left alone and is yet unable to enjoy the excitement he craves. As a result he grows increasingly restless and irritable, dominating the whole household, till finally exhaustion produces the refusal of food, wakefulness, dyspepsia, and a whole train of other difficult symptoms.

In older children the line which separates fractiousness and naughtiness and restlessness from definite neuropathy begins to be more marked. The nature of the infant and young child taking its color from its surroundings is sensitive, mobile, and inconstant. With every year that passes, the normal child loses something of this impressionable and fluid quality. Increasing experience and intellectual development if tempered with discipline give the child a more and more unyielding surface to environment until finally it becomes set in the stability of mature age.

In the passage from early infancy upward, we can recognize a gradual approach to the conditions of adult life if things progress normally; but when at any stage we can perceive a lagging backward, a tendency to fixation in early phases of development, then we are sure that things are going amiss. Fractiousness, naughtiness, violent paroxysms of temper, uncontrollable weeping, morbid fears and inclinations should vanish away with the first years of life. If they persist into later childhood, we shall see that in a large percentage of cases definite neuropathy is well under way. When we pause to examine these children we see as the fundamental feature clearly portrayed, the elements I am repeating so many times; marked sensibility to all forms of stimuli with an incapacity to control emotional responses—typical reactions of the first period of life before the molding forces of discipline and the experiences of reality have had their play. Looking more carefully into their natures, one observes that the emotional component of their being has so overgrown itself as to dominate their lives in spite of every effort at control. "Broadly speaking, there are two types of neurotic children," says Leonard Gutherie, who has described them perhaps better than anyone else, in his work on *The Functional Diseases of Children*, "the restrained and unrestrained type. In the latter there is supersensitiveness and excessive reactions to all forms of stimuli. Their emotions are easily excited, and they have little control over their outward display. Their feelings are strong for the moment but shallow and changing;

some are extravagantly affectionate at one moment, brutally callous and indifferent the next, selfish beyond measure, craving for sympathy, regarding themselves aggrieved if every whim of the moment is not satisfied, goaded to fury by interference, and resentful of all discipline. They are high spirited and impulsive, but easily discouraged, now enthusiastic and castle building, and now crushed and abased, worried by trifles, anticipating difficulties but making no effort to meet them. Often they are timid, fickle, untrustworthy, imaginative, and superstitious. They are quick at learning but forgetful of facts, seldom capable of prolonged industry, hating drudgery, but working with feverish energy in fits and starts; they are speedily exhausted both bodily and mentally. They are continually seeking new forms of emotional and mental excitement; and unless these are provided for them, they become bored, morose, and hypochondriac. They never seem to learn prudence or common sense and caution from experience and their actions are capricious and eccentric."

Of the restrained type he says: "As in the first there is supersensitiveness to all forms of stimuli, but the reactions are suppressed. Emotions are strongly felt, but the control over their outward display is equally strong. They are regarded as wanting in natural affection, but really yearn to be loved; they brood over slights and become gloomy, morose, solitary in habits, introspective, and superstitious. They harbor various kinds of phobias. Their apparently stolid indifference to their surroundings is varied by sudden fits of ungovernable rage or weeping. Some are observant and intelligent but so reticent that they pass for being sullen or obstinate. This disposition with its characteristic suppression of all outward emotion is as exhausting as that of the other type, in which emotional excess is obvious, and it is associated with many similar complaints."

This, then, is the picture of the neurotic child, always a prey to and driven by unbridled emotions, never able to harmonize the internal mental life with external reality, ever the subject of psychic conflict and strain, and perpetually a sufferer from numerous functional disturbances. Many of the most troublesome disorders encountered in children are met in these patients. They are liable to repeated night terrors, somnambulism, headaches, migraine, various forms of tic and bad habits, phobias and obsessions, cold extremities and poorness of circulation, eczema, urticaria, and erythema in its varied forms, cyclic vomiting, and cyclic or postural albuminuria, enuresis and lienteric diarrhea, alternating with constipation and mucous colitis. If rheumatic, they are very prone to develop chorea severe out of all proportions to any cardiac or arthritic symptoms that may be present. At an early period of their lives they are usually branded as having weak hearts, weak lungs or weak digestions or tendencies to consumption, and are treated with the utmost deference and consideration in view of such

vague proclivities, until they become introspective, hypochondriac, neurasthenic, psychasthenic, or hysterical.

These symptoms are so common that every physician is called daily to treat them, and in many instances are without any physical basis and, like functional disturbances of any nature, yield very poorly to medical treatment. It is well recognized, however, that physical causes are present as an important etiological factor in some cases. The so-called postinfective neurosis of children is a common thing, and organic heart or kidney disease, severe nutritional disturbances, errors of internal secretion, visual defects and pathology in the nasopharynx, do sometimes produce rather marked nervous symptoms; but usually these things, if present at all, play only a subordinate rôle, and if attention is directed to them alone, disappointing results are the rule.

I cannot close better than quoting again from Cameron, the great master in the field of nervous children. He says: "And so we come back to the point from which we started: the nervous infant, restless, wriggling, and constantly crying! The nervous child, unstable, suggestible, passionate, and full of fears! The nervous schoolboy or schoolgirl prone to self-analysis, self-conscious, and easily exhausted! Refusal of food, refusal of sleep, negativism, irritability and violent fits of temper, vomiting, diarrhea, morbid flushing and blushing, habit spasms, phobias, all controlled not by reproof or by medicine, but by good management and a clear understanding of their nature."

The hygiene of the child's mind is as important as the hygiene of the child's body and both are studies proper for the doctor. Neuropathy and an unsound nervous organization are often enough legacies from the nervous disorders of childhood.

624 METROPOLITAN BUILDING

BENIGN OR FUNCTIONAL ALBUMINURIA IN CHILDREN

Further Studies

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THE significance of albumin in the urine of apparently healthy children and young adults is still the subject of much discussion. Most of these cases are accidentally discovered in the routine examination of urine in schools, orphan asylums, dispensaries or office practice. This so-called benign albuminuria is not an uncommon finding in children, occurring much more frequently than in adults. The literature on this subject has been summarized during the past ten years by Lauener,[1] Calvin, Isaacs and Meyer,[2] Ashburn,[3] Fishberg,[4] Palmer,[5] Diehl and McKinlay,[6] Hellebrandt,[7] Jamieson and Scott[8] and others.

The outstanding observations are that slight or moderate albuminuria is a fairly frequent occurrence in children, especially in those over six years of age. It becomes more frequent toward puberty and reaches a maximum incidence during adolescence, the period of greatest growth. The incidence appears to be higher in girls. Globulinuria is the type of proteinuria that predominates in these cases although serum albumin may occur alone even in benign proteinuria. The acetic acid body (cloud forms in cold urine after addition of a few drops of 5 per cent acetic acid), considered as mainly euglobulin, is usually present.

In recent years physicians generally have accepted the fact that albuminuria in children may be and usually is benign and have refrained from unduly arousing anxiety in themselves or the parents of their patients, abandoning the axiom that "albuminuria is a sign of Bright's disease until proved otherwise." Nevertheless, it is not a symptom to be disregarded, as the diagnosis of "physiologic albuminuria" is never entirely satisfactory even in cases of children apparently in the best of health. Consequently, studies concerning the etiology of the condition are still being pursued. A summary of these may be found in the aforementioned literature.

A factor which undoubtedly is the cause of a certain percentage of proteinuria, especially in young male adults, but which is scarcely mentioned and seldom discussed in the literature, is the prostatic and seminal vesicle secretions leaking into the urethra and mixing with the urine. Belfield[9] and Rolnick[10] have pointed this out, but it has escaped general attention. They state: "It is known that the normal semen con-

From the Children's Department of the Cook County Hospital.

tains albuminoid bodies of two classes: (1) globulins, which like serum albumin are coagulated by heat or nitric acid; and (2) other proteins, which are precipitated by nitric acid but not by heat. If normal semen is mixed with ten times its bulk of water and filtered and nitric acid is allowed to flow down the side of the test tube containing the filtrate, three phenomena usually appear: (1) a white coagulum of globulin at the bottom of the tube, like coagulated albumin in the urine of persons with chronic nephritis; (2) above this a clear fluid for 1 or 2 inches, and (3) still higher a diffuse white cloud of proteins, which disappears on gentle heating and reappears on cooling. This 'vesicular albuminuria' is easily mistaken for renal albuminura." They often obtained a positive test for protein in the urine after massage of the vesicles, especially in chronic vesiculitis, even though the urine passed before the massage did not give a positive protein reaction. They conclude "the proteins secreted by the epididymis and seminal vesicles and passing thence into the bladder may be sufficient in amount to show a precipitate in the urine by heat and nitric acid, although urine obtained at the same time through ureteral catheters may not show any."

OBSERVATIONS ON SIXTY BOYS

In order to determine the importance of this factor in the so-called benign albuminurias of children the author undertook an investigation on fifty boys ranging in age from five to twelve years. The urines of these boys were examined on three successive mornings and evenings and found free of protein by the usual nitric acid and heat-and-acetic acid tests. The boys were then subjected to gentle manual prostatic and vesicular massage for from five to ten minutes. All the urine passed during the next three hours was examined. In none was a positive protein test obtained either by the addition of nitric or acetic acid to the cold or warmed urines. The same procedure was carried out on ten boys showing benign albuminuria. No increase of the amount of albumin was noted after the massage.

TABLE I

SUMMARY OF EXPERIMENT

NUMBER OF BOYS STUDIED	AGE RANGE IN YEARS	URINE EXAMINATION 3 SUCCESSIVE A.M. AND P.M. SPECIMEN BY HEAT AND ACETIC, AND NITRIC ACID TESTS	PROCEDURE	URINE PASSED WITHIN THE NEXT THREE HOURS
50	5-12	Negative for protein.	Digital prostatic massage 5 to 10 minutes.	Negative for protein.
10	8-13	Trace to 2+ protein.	Digital prostatic massage 5 to 10 minutes.	Trace to 2+ protein. Same amount as before massage.

SUMMARY AND CONCLUSIONS

The author believes that prostatic or vesicular protein secretions in boys before the age of puberty play no rôle in the high incidence of benign albuminuria in children. That this factor requires further study in male adolescents and young adults is obvious, and the hope is entertained that the degree to which vesicular albuminuria plays a rôle in the incidence of albuminuria in young adults will be determined by those who have the proper material available for study.

Although the significance of albuminuria in children and young adults still remains obscure, recent contributions are gradually elucidating some of the factors involved. The author after paying particular attention to this type of case for the past eight years feels as he did in 1926, that most of these albuminurias in otherwise healthy children are harmless, benign, and relatively transient, that the condition should not be stressed either to the parent or patient, as the "disease" often occurs only in the physician's test tube. Yet the physician cannot totally disregard this benign albuminuria. Every case should be under observation for a variable period until it is certain that no organic changes have occurred, (such changes as indicated by the appearance of casts, hematuria, fixation of specific gravity and hypertension) and the albuminuria has subsided. Neither rest cures nor low protein diets should be prescribed. Other abnormalities such as malnutrition, defective posture, and foci of infection, if present, should be treated as usual.

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THE USE OF COPPER AND IRON IN THE TREATMENT OF SECONDARY ANEMIA IN CHILDREN

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THE value of the administration of copper in conjunction with iron in the treatment of secondary anemia has been demonstrated in animals,[1-8] in children,[9, 10, 11, 12] and in adults.[13] But more observations are needed on the ratio of copper to iron, and also on the comparison of the effects of cupric and ferric compounds, and cuprous and ferrous compounds, because of the reports that the latter are more efficacious.[14, 15, 16] Six children suffering from secondary anemia due to malnutrition or infections, whose hemoglobin varied from 40 to 74 per cent (average 58.5 per cent) on admission were treated. Three times daily they were given from 5 to 10 c.c. (according to their ages) of a solution containing 0.5 gm. of cupric sulphate and 10 gm. of ferric ammonium citrate per 100 c.c. of 25 per cent aromatic elixir solution (U.S.P.). Such a preparation can be prepared at a cost of less than twenty cents per pint. In this way, each patient received daily from 10 to 20 mg. of copper and from 250 to 500 mg. of iron, which is in agreement with the dosage of iron found to be optimal by Minot and Castle.[17] Similar commercial preparations were considered, but the majority of these contained less than one-third of these amounts of copper and iron, and the costs were many times higher. Different proportions of copper and iron were used at first in order to determine a palatable ratio. It was found that a proportion (of available copper to iron) higher than 1 to 25 produced nausea and vomiting in 20 per cent of the patients.

Six children whose secondary anemia was similar to that of the first group and whose hemoglobin on admission averaged 63 per cent were given cuprous and ferrous glutamate.* This material was made up in capsules each of which contained 30 mg. of cuprous glutamate and 750 mg. of ferrous glutamate. The dosage was three capsules daily, which provided the same amount of iron as 15 c.c. of the cupric and ferric compound. The ratio of available copper to iron was 1 to 34.

The hemoglobin content of these children was determined at intervals for an average of four weeks by the Sahli method and recorded on a

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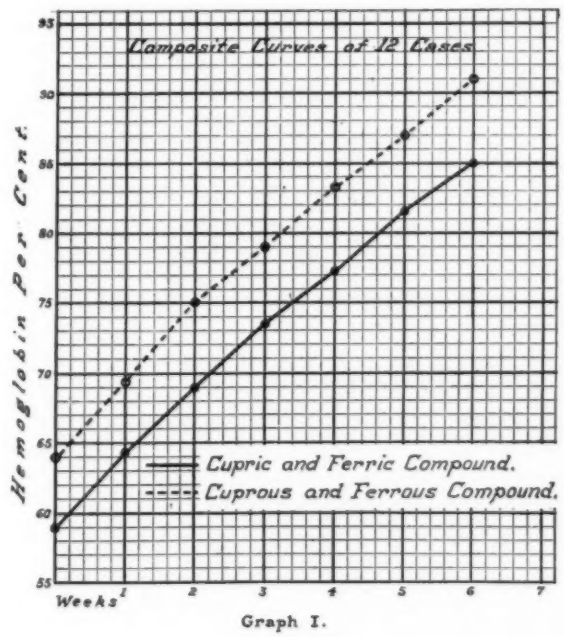
*The cuprous and ferrous glutamate was kindly furnished to us for this purpose by the Calco Chemical Company.

percentage basis, 16 gm. hemoglobin per 100 c.c. of blood being regarded as 100 per cent. While the children were in the hospital, examinations were made at least once a week, but those observed in the dispensary had their examinations at longer intervals. Probably the curve of rising hemoglobin would have been sharper in its earlier stages, if determinations had been made at more frequent intervals.

In the children whose anemia was due to malnutrition the hemoglobin content increased rapidly; while in those who had infections, the rise usually did not occur until the infection had subsided.[18, 19, 20] As may be



Graph I.

seen in Graph I, the children treated with the cupric and ferric compound, and those given the cuprous and ferrous compound showed the same rate of increase in hemoglobin content, namely 4.6 per cent per week.

CONCLUSION

As far as can be judged from this small series observed for a short period of time, a ratio of copper to iron of 1 to 25 is palatable and does not cause nausea; and a cupric and ferric compound is as efficacious in the treatment of secondary anemia in children as is a cuprous and ferrous compound.

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DIABETES MELLITUS IN CHILDREN

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SIXTY-FIVE children with diabetes mellitus were admitted to the wards of the Children's Memorial Hospital during the period from April 1, 1921, to November 1, 1933. This number includes ten private patients and fifty-five patients admitted through the Out-Patient Department, where during the same period a total of 85,359 children were registered. Since November, 1926, I have had the opportunity to observe and treat fifty-two of these children.

Since in juvenile diabetes the pathologic changes in the pancreas are not readily demonstrable[1] and do not seem sufficient to account for the severe disturbances of metabolism, it seemed possible that a study of this disease in children, in whom the course in untreated cases is very rapid, might throw some further light on the underlying, as well as the exciting causes of the disease.

In the survey of these cases, the incidence of the disease was studied in relation to age, sex, and nationality. The effect of heredity as a causative factor and the influence of infection, trauma, and carbohydrate overfeeding as exciting factors were noted in the fifty-two patients. Several glucose tolerance curves showing the course of the disease over a period of years were plotted. A detailed analysis of the fatal cases was attempted.

AGE AT ONSET OF SYMPTOMS

The highest incidence of onset in this study is in the second and fifth years of life. It is possible that the high carbohydrate diet in the latter part of the first year is a contributing factor to the high incidence of appearance of symptoms in the second year although a history of heredity was noted in two such instances. A grandaunt of a twenty-month-old boy had recently developed diabetes. A paternal uncle of an eleven-month-old boy had recently developed diabetes at the age of thirty-nine years. A small pancreas was reported at autopsy in this latter child.

Cammidge[2] suggests that the disease may develop from inherited defects in the pancreas, recessive in nature, "which prevent the development of the organism in a particular direction from keeping pace with the increasing demands of the growing body, and as the inherited factor probably differs in intensity, so the period of life at which the symptoms of diabetes appear also varies." Trusen and Walenta[3] found

From the Children's Memorial Hospital.

that the greatest number of cases appeared in the sixth year and attributed this to the greater exposure of the child to infection on entering school. Priesel and Wagner[3] reported a large number of cases appearing in the sixth year, but a still larger number at puberty. White[4] observed a marked increase in the disease at puberty, and attached much importance to the overheight and functional overstrain of the organism at this period as etiological factors.

TABLE I

AGE AT ONSET OF SYMPTOMS OF DIABETES MELLITUS IN 65 CHILDREN

AGE IN YEARS	NUMBER OF CASES
0-1	2
1-2	11
2-3	7
3-4	0
4-5	8
5-6	5
6-7	4
7-8	4
8-9	7
9-10	5
10-11	3
11-12	4
12-13	5

SEX

Of the sixty-five cases, forty-one, or 63 per cent, were males and twenty-four, or 37 per cent, were females. The preponderance of boys over girls is greater than that usually reported. In Joslin's[5] group of 395 children, 52 per cent were males and in his 2,800 adult cases, 57 per cent were of this sex.

NATIONALITY

As shown in Table II, the incidence of the disease was highest in northern Europeans especially those of Scandinavian extraction. This may be explained in part by the author's observation that the usual Scandinavian diet contains a high proportion of carbohydrates. However, this high incidence may be due to the relatively larger proportion of northern Europeans residing within a reasonably short distance from the hospital. The markedly low incidence of diabetes among the Jewish race in this group may be due to the relatively small attendance of Jewish children at this clinic. Furthermore, diabetes in the Jew tends to be inherited as a dominant characteristic and less frequently develops in the very young child. The difference in the statistics of Priesel and Wagner[6] who reported 30.6 per cent Jews among 121 patients and those of Joslin[5] who reported only 6.1 per cent Jews in a large series probably lies in the difference of the Jewish populations of Vienna and Boston.

TABLE II

NATIONALITY OF 47 PATIENTS STUDIED

NATIONALITY	NUMBER OF CASES
Scandinavian	14
German	7
Irish	6
Polish	6
French	2½
Italian	2
Scotch	2
Dutch	2
Hungarian	2
Bohemian	1
Hebrew	1
Austrian	1
English	½
Negro	0

HEREDITY

A careful history of diabetes in the family and relatives was elicited. In eleven, or 21 per cent of the fifty-two children, a history of the disease in relatives, with two instances in an older brother, was obtained. Diabetes developed in a father five years after the appearance of the disease in a ten-year-old daughter. The incidence of a history of diabetes in the family or other relatives varies greatly in the reports from different clinics—in some instances, where the patients have been followed for several years, it reaches almost 50 per cent.[7]

Buchanan,[8] in a clinical study, felt that diabetes was not transmitted as a Mendelian characteristic. He studied the descendants from the marriage of a diabetic and a nondiabetic individual through the second and third generations in thirty-four families. Cammidge[2] concluded from clinical studies and experiments with interbreeding of races of mice and of other animals, with normal and high blood sugars, that diabetes is transmitted as a recessive characteristic, but can also be inherited as a dominant one. In the recessive type, the disease occurs early in life, is usually severe and progressive, and frequently self-exterminative; while in the dominant type it usually appears after 40 years, is almost invariably mild, and may persist for years without causing serious symptoms. In both types, the disease manifests a tendency to develop earlier in successive generations.

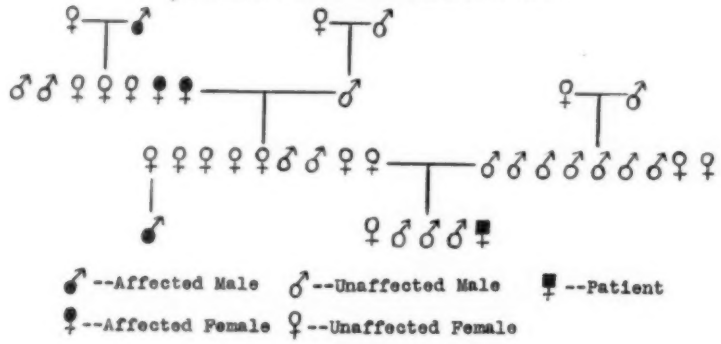
D. B., a girl with onset of symptoms at twelve years and two months, had a maternal grandmother and a maternal grandaunt with diabetes (the former died at the age of forty-one years after six or seven years of the disease), and a maternal great-grandfather who died of diabetes. A male maternal first cousin has recently developed diabetes at the age of fourteen years. The girl's mother, aged fifty-five years, has no symptoms of diabetes and the paternal history is free of the disease. If we accept Mendel's Law in the inheritance of dia-

betes, then the father must have been a hybrid character since the mother evidently was a hybrid carrier capable of transmitting the disease. This family tree would seem to illustrate the recessive type. The course of the disease in this child was mild for about three months and then became quite severe following an upper respiratory infection. She died at the age of thirteen years, ten months after the onset of symptoms.

Wright[9] demonstrated cases of dominant and recessive hereditary types. Curtis[10] from a study of diabetic twins felt that the major feature of the disease pointed to a hereditary background or to some congenital liability to functional failure of the islands of Langerhans. In accord with this view, Priesel and Wagner[6] believe that the exciting factors which precipitate diabetes do so because of a preexisting anlage which

TABLE III

HEREDITARY AND FAMILIAL HISTORY OF D. B.



is often manifested by some external stigmata of degeneration. Colwell and Bright[11] suggest as a result of experiments on the effect of epinephrin on glucose oxidation "that ordinary diabetes mellitus is the result of a functional disorder of the pancreas, which is dependent on a disease of the sympathetic nervous system, and that continuous excessive secretion of epinephrin may be an important intermediate factor in this mechanism." Of interest in this connection is the recent report of the discovery by Medvedeva[12] of a hypoglycemic hormone of the cortex of the adrenal gland. Houssay and Biasotti[13] found that the blood sugar was not influenced greatly in pancreatectomized animals which had also been hypophysectomized, that insulin shock was more readily produced than in the normal animal, and later that glycosuria could be produced by injection of an anterior lobe hormone. They concluded that the anterior lobe hormone acts directly on the tissues, stimulating the production of sugar and perhaps retarding its consumption when insulin is lacking.

EXCITING FACTORS

Carbohydrate overfeeding, trauma, and infections have been frequently emphasized as exciting factors in precipitating diabetes. Overfeeding may have been a factor in the case of a ten-year-old girl whose diet had consisted of a combination drug- and grocery-store fare of few cooked meals and many malted milks. She complained of upper abdominal pain—possibly cholecystitis—for one year prior to onset of diabetes. Her father has since developed the disease, five years after onset in the child. A boy of five years developed diabetes during the course of an acute otitis media. He had consumed four or five glasses of malted milk each day for several months in order to consume a quart of milk daily. The father of an eight-and-one-half-year-old boy had died from a carbuncle, and the child had been placed in an orphanage where he had a high starch diet for eighteen months. He had many attacks of bronchitis during this period. His course is shown on Chart 3. A boy with onset of diabetes at twenty-three months had had an inadequate diet of condensed milk, potatoes, and gravy to which bacon was added at twenty-one months. A five-year-old boy, born in Italy, who had had a mild diabetes for one year, stuffed his pockets with sweetened figs, and drank the customary glass of wine with each meal.

In two instances, trauma preceded the onset of diabetic symptoms. A four-year-old girl fractured her right radius one month before onset of symptoms. A foreign body was removed from the esophagus of a two-and-three-quarter-year-old girl, one year prior to onset of symptoms. The foreign body had been present for several weeks with a resulting anorexia which had persisted up to the development of diabetes and for many weeks thereafter. She contracted a severe cold about a month before onset of symptoms.

In four other children, infection may have been an exciting factor. A six-and-three-quarter-year-old girl developed symptoms of diabetes two months after the onset of a severe attack of tonsillitis from which she had not yet completely recovered. Her mother had a thyroid adenoma, had had two miscarriages, and while pregnant with this child had pernicious vomiting. Measles preceded the onset of symptoms less than two months in a two-year-old boy. A peritonsillar abscess ruptured spontaneously in an eleven-and-three-quarter-year-old girl one month prior to onset of symptoms. Varicella preceded the onset of symptoms less than one month in a two-and-one-half-year-old girl. In two instances the disease was discovered during the course of an acute otitis media. Acute purulent otitis media was present in three other children upon initial admission to the hospital although symptoms of diabetes had been present earlier. Toverud[14] found a recent history of infection in 26 per cent of his cases and felt infection was of greater importance than heredity in the causation of diabetes in children. Wil-

liams and Dick[15] noted frequent glycosuria and hyperglycemia during the course of acute infectious diseases.

Metabolic disturbances are frequently found in the family history and occasionally in the child's history. Two children developed symptoms of diabetes at one and one-half and two and one-fourth years shortly after the subsidence of a moderately severe eczema. A boy, five and three-quarter years old, who had been breast fed until eighteen months of age and who is said to have been a "skeleton," had both parents with thyrotoxicosis. An older brother has recently developed diabetes. Other instances of asthma and thyroid disturbances in the family histories were found.

It is difficult to draw conclusions from the above as to importance of carbohydrate overfeeding, trauma, infection, and metabolic disturbances in the production of diabetes. Prolonged overfeeding with carbohydrates in several instances, the presence of infection within two months of the onset of symptoms of diabetes in three instances, and concomitant with onset of symptoms in two cases suggests a close relationship between these factors and the onset of the disease.

TOLERANCE

In the past, juvenile diabetes was considered a progressively deteriorating disease ultimately approaching a total diabetes. With the discovery of insulin hope was aroused that this spectre would disappear, and indeed many children showing great gains in tolerance with its use have been reported. Roberton[16] recently has stated that diabetes is a progressive disease tending to approach totality. He calculated, in a large group of collected cases, the ratio of potential carbohydrate in the diet to the insulin required to keep the urine sugar-free. He calls this the C/I ratio and found, using Woodyatt's[17] determination, that 1 unit of insulin has the power to burn 1½ gm. of glucose and that the glucose tolerance tended to fall to a level of 1.5 or absolute diabetes.

In my series, in which the diets were higher in carbohydrates with a ratio of fatty acid to glucose of 1:1, only a few of the cases fell below 3, calculated according to Roberton's method. Possibly a longer period of observation might show a lower figure.

Collens and Grayzel[18] found the glucose-insulin ratio of particular value in indicating the course of the disease. They determined this ratio by dividing the amount of glucose utilized by the amount of insulin required to keep the urine sugar-free. I have found the determination of glucose tolerance helpful in prognosis and management of the individual cases. In determining the tolerance, 1 unit of insulin was considered sufficient to burn 1¾ gm. of glucose; the number of units of insulin administered was multiplied by 1¾ and the product in grams subtracted from the total glucose of the diet, the remainder being the amount of glucose metabolized, where the urine was sugar-

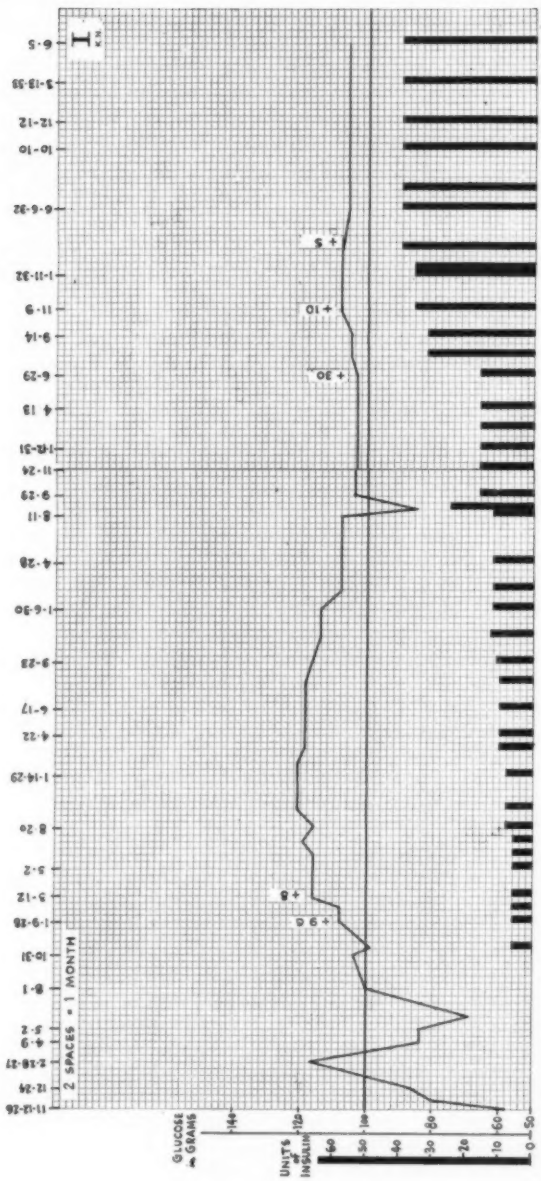


Chart 1. K. N. Solid line represents the total available glucose of the diet in grams. The vertical blocks represent the insulin dosage. Plus or minus "g" denotes the addition or subtraction of glucose from the diet. The drop in the tolerance curve on February 28, 1927, was due to persistent upper respiratory infections and that of August 11, 1930, to a severe diarrhea.

free. The usual tolerance curve in this series shows a rapid rise in the first two months of insulin treatment, a slight drop at six months, and a tendency thereafter to remain above 100 gm.

Marked permanent losses of tolerance were noted in one case after an attack of scarlet fever complicated in the second week by suppurative appendicitis and peritonitis, and in a case of protracted bronchitis. Great temporary losses of tolerance were seen in two cases of lung abscess with empyema.

The charts show the fluctuations of the glucose tolerance under insulin management, the effect of intercurrent disease, and the effect of dietary indiscretions in this series.

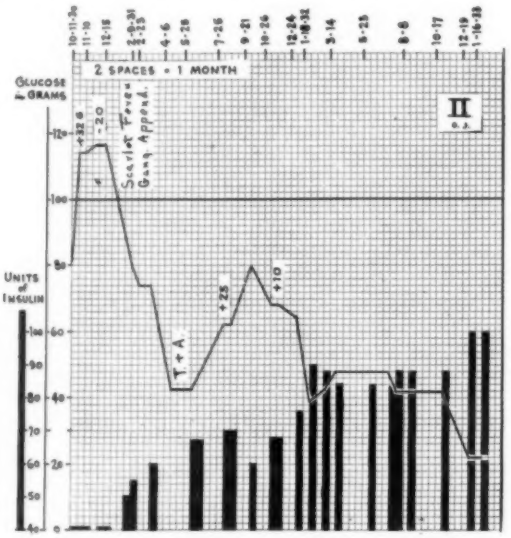


Chart 2.

Chart 1 shows the fluctuation of the glucose tolerance during six and one-half years of treatment. No insulin was administered during the first year; the fluctuations were marked because of repeated upper respiratory infections. The drop on August 11, 1930, was due to severe diarrhea.

Chart 2 illustrates the damaging effects of scarlet fever and peritonitis on the tolerance, with improvement after tonsillectomy. There is a gradual but continuous fall in the curve due in part to the economic stringencies during the latter part of 1931 and 1932. This case tends to approach total diabetes.

Chart 3 illustrates a mild case of diabetes in a boy now twelve years old. There is a marked drop in tolerance with the development of a

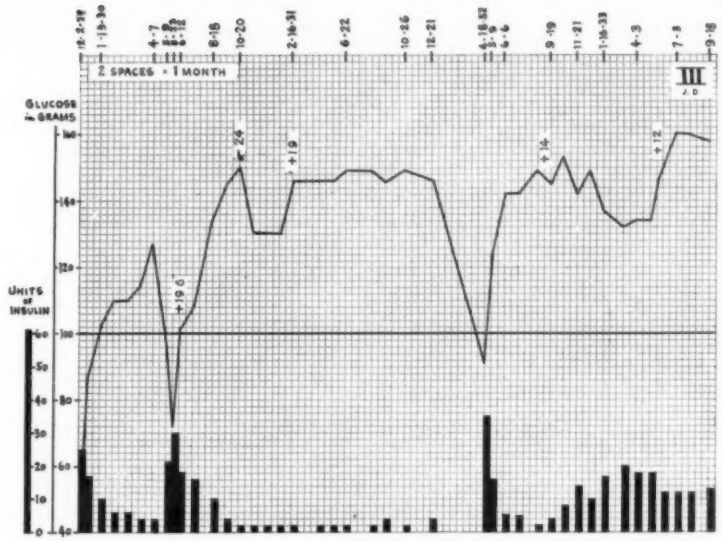


Chart 3.

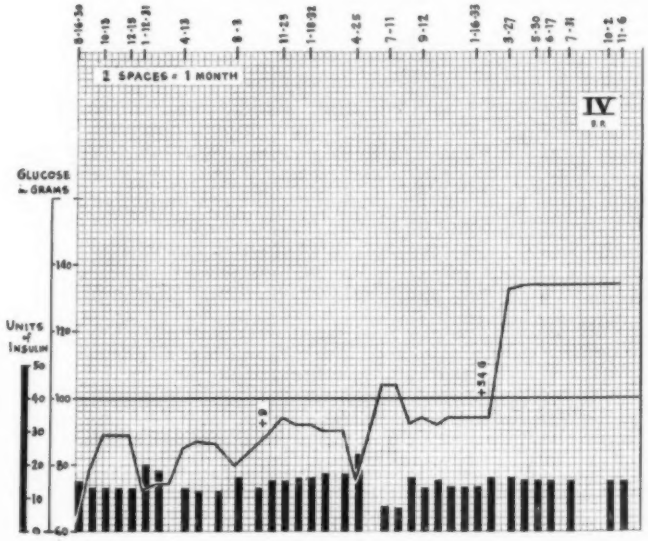


Chart 4.

lung abscess with empyema, which was preceded by a mild attack of scarlet fever following tonsillectomy; the second sharp drop in the tolerance was due to a voluntary reduction of the diet, and the third sharp drop to a break in routine care at home. Prompt rise in tolerance followed increased diet and insulin.

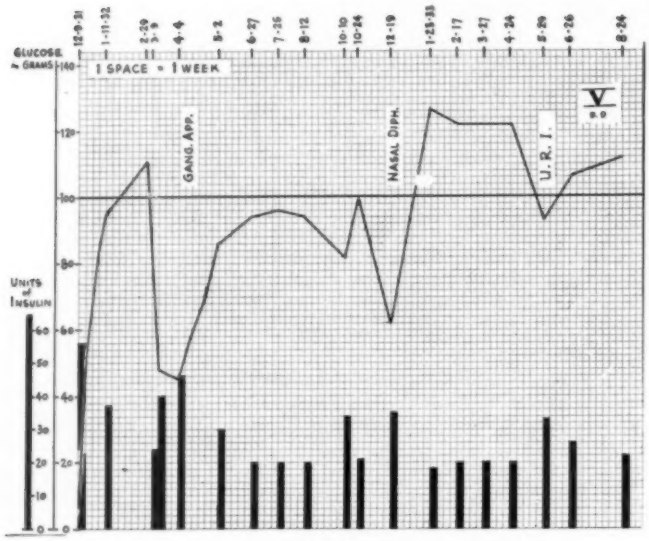


Chart 5.

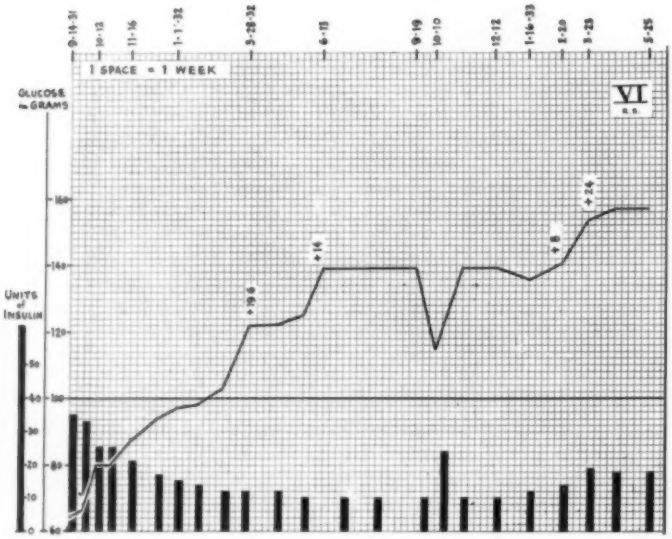


Chart 6.

Chart 4 shows little fluctuation of tolerance over a period of two years in a boy whose age at onset was one and three-quarter years. After the addition of a large amount of carbohydrate to the diet during the past year, there has apparently been an amazing increase in the tolerance.

Chart 5 shows the depressant effects of gangrenous appendicitis and the lesser effects of nasal diphtheria in a four-year-old boy. Diabetes had been present for two years, under haphazard control for one year.

Chart 6 shows the curve of a mild case of diabetes in a four-and one-fourth-year-old boy whose symptoms were first noted two weeks previously. Tolerance was lowered temporarily in November, 1932, because of an upper respiratory infection.

Chart 7 illustrates a very mild case of diabetes in a five-year-old girl with a remarkable return of tolerance.

The case illustrated in Chart 2 tends to approach total diabetes. Children who have not followed a proper diabetic regime are apt to

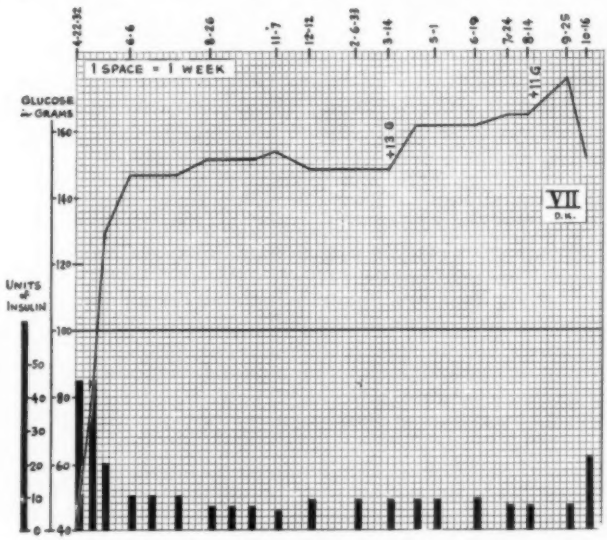


Chart 7.

approach totality. It is often impossible to chart their progress since the urine is rarely sugar-free over long periods. In the cases where the regime is poorly controlled and in the severest cases, xanthosis[19, 20] is a prominent feature.

MORTALITY

When the older literature prior to the discovery of insulin is studied, one is impressed with the hopeless outlook in juvenile diabetes. Fowler[21] in 1892 said, "A peculiarity presented in children is the rapidly fatal course. No recoveries have been reported. In fact the disease is here very rapidly fatal. So rare is diabetes in childhood and infancy that few of the textbooks devoted to pediatrics mention it at all." In 1872 Senator[22] said that the prognosis was hopeless and the treatment use-

less. Osler[23] stated in 1917 that he personally had not known of a case of recovery in a child. In his book of the same year, Holt[24] wrote that in few diseases has the prognosis been so bad as in diabetes in children, but that the outlook was not so immediately dark as it had been because of the recent methods of treatment, especially that recommended and elaborated by Allen. Statistics from Joslin's large series and from the Mayo Clinic showed a mortality of two-thirds of their cases in the eight years and three years, respectively, just preceding the discovery of insulin.

A study of the recent literature changes the picture completely. Joslin and White[25] in 1928 gave a mortality rate of 1 per cent per year for 303 patients over a period of twenty-two months. Allan and Wilder[26] report a mortality rate of 1.3 per cent for that year. Both Joslin and Wilder report a mortality rate around 9 per cent and stress the fact that the well-educated diabetic rarely dies of diabetes. Priesel and Wagner found less than 1 per cent mortality in 121 cases, while Trusen and Walenta[27] report a mortality rate of almost 50 per cent. A great portion of their fatal cases resided in rural districts where it was not possible to manage the complications promptly. Toverud[14] in Norway reported a 36 per cent mortality rate, which he attributed to the inaccessibility of the clinic to the patients living among the fjords and other distant parts of that country.

Of our group of fifty-two children with onset between the ages of ten months and twelve and one-half years, who have been under observation from three months to six and one-half years, there are forty-five living, two in whom contact was lost, and five dead. The analysis of the fatal cases follows:

D. B., a girl, after ten months of diabetes, was readmitted to the hospital in semicoma, maniacal, with a blood sugar of 0.533 gm. per 100 c.c. of blood and plasma CO_2 of 13 volume per cent. The mother had been working out of the home on the day of the onset of this acute illness, which began with vomiting. The child had retained no food for 36 hours, and no insulin had been given during this time except for the 20 units given shortly before admission. There was little response either in the blood sugar or CO_2 to 90 units of insulin administered in the hospital. She expired twelve hours after admission with cyanosis and a pulse rate of 180 per minute. Death was attributed to heart failure as a result of ketosis. The death of this thirteen-year-old child was the result of imperfect understanding of the seriousness of the symptom of vomiting and indicated the necessity of education of at least two persons in the home, in addition to the patient, in the treatment of diabetes in children. Insufficient insulin was given this child.

Infection was a major factor in the death of two other children. W. W., a ten-month-old boy, was admitted with a diagnosis of acidosis. A marked glycosuria was discovered and controlled with insulin although the infant had many insulin reactions. After the fifth hospital day, diarrhea, bronchitis, and otitis appeared, and the child expired from acute intestinal intoxication on the twelfth day. The post-mortem examination revealed a gross atrophy of the pancreas without any microscopic changes. A paternal uncle of this boy died at the age of thirty-nine years of diabetes.

D. K., a girl, aged four and three-fourths years, was admitted to the hospital with a history of diabetes of one month's duration, a cough and a cold for one week, and acidotic poisoning for thirty-six hours. She had received 105 units of insulin but died twenty-six hours after admission with a diagnosis of right lower lobar pneumonia and coma. No chemical determinations of the blood had been made. At the autopsy extensive bronchopneumonia of both lower lobes, a tracheitis, and hydropic and lymphocytic changes in the islands of Langerhans were revealed.

A. K., an extremely emaciated boy, aged eight and one-fourth years, had had symptoms of diabetes for three months and acidosis for twenty-four hours. Upon admission the blood sugar was 0.460 gm. per 100 c.c. and twelve hours later was 0.700 gm. During the seventeen hours in the hospital 170 units of insulin were administered. Cerebrospinal fluid postmortem was 0.187 gm. per 100 c.c. No autopsy was permitted.

E. B., a boy, aged eight and three-fourths years, was dying when admitted to the hospital. He had a history of diabetic symptoms for two weeks and acidosis for two days. The skin was cold and dry; pulse was imperceptible at the wrist; blood pressure was not measurable; and the heart tones were very distant and irregular. During the three hours that he lived in the hospital, he was given 140 units of insulin, glucose intravenously, fluids subcutaneously, caffeine and heat. The urine contained 4.2 per cent glucose, and the postmortem plasma CO_2 was 17 volume per cent. In these last two cases, it seems possible that irreversible changes may have taken place before treatment was instituted.

Larger doses of insulin administered early in the disease should have influenced the outcome favorably in at least two of the fatal cases.

From the above findings, it should be emphasized that any change in the condition of the patient should be promptly reported to the hospital or the physician, that continuous and unremitting education in the use of insulin and diet is imperative, and that patients with intercurrent infections should be under close medical observation.

SUMMARY

1. Sixty-five children with diabetes mellitus were studied to determine the age at onset of symptoms, the sex, and the nationality. Fifty-two of these children were treated and observed for periods varying from three months to six and one-half years.

2. The incidence of onset was high in the fifth and ninth years but highest in the second year of life.

3. Sixty-three per cent were males.

4. Scandinavian nationalities predominated.

5. Eleven patients, or 21 per cent, had a history of diabetes in ancestors or immediate family. Heredity seemed to be an important factor in the development of the disease.

6. Infection and overfeeding were important causes in precipitating the onset of symptoms. Serious infection was present at the onset in many instances.

7. The tolerance for glucose under treatment tended to remain above 100 gm. unless severe infection or prolonged dietary indiscretions occurred. Tolerance did not fall in the cases that were well controlled.

8. Five children died of diabetic coma in the hospital. Only one of this number had previously been treated in the wards of the hospital.

Invaluable assistance was given me by the Social Service Department and the Dietetic Service of the Hospital.

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BACILLUS ENTERITIDIS MENINGITIS IN AN INFANT OF FIFTEEN MONTHS

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IN 1930 Lynch and Shelburne[1] reviewed the cases of meningitis caused by bacilli of the paratyphoid group. Despite the numerous reports on record, they accepted only fifteen cases in which identification of the organisms was based on indisputable cultural or serologic evidence. They added a sixteenth case due to the *Bacillus enteritidis* of Gärtner and concluded that meningitis due to bacilli of this group is a serious condition, usually fatal, and should be suspected whenever gram-negative motile rods are found in the cerebrospinal fluid.

Cooke and Bell[2] emphasized the fact that meningeal infection by organisms of this group is sharply limited to early infancy. The majority of the patients noted by other observers are under one year of age. As an explanation of the age incidence, they suggest three factors: (1) the greater permeability of the intestinal mucosa in early infancy; (2) decreased resistance of young infants to bacterial infection associated with defective antibody formation; and (3) the influence of digestive disturbances and malnutrition on the above mentioned factors.

In a recent review of 705 cases of meningitis occurring in children, Fothergill and Sweet[3] stated that organisms of the colon group caused nine of the cases. Eight of these patients were under five weeks of age. A bacteremia was almost universally present. In the majority of cases there was a relatively high percentage of mononuclear cells in the spinal fluid compared to other types of purulent meningitis.

The variable symptomatology of infection with *Bacillus enteritidis* in older individuals is well illustrated in the case reported by Mc Nee.[4] His twenty-five-year-old male patient presented the picture of influenza complicated with pneumonia and acute hemorrhagic nephritis. No diarrheal symptoms occurred. The pus expressed from the bronchi at autopsy revealed an almost pure culture of *Bacillus enteritidis* as did a culture from the spleen. Cerebral edema was present but there was no evidence of purulent meningitis.

One hundred consecutive cases of meningitis observed from 1927 to 1931 at the Los Angeles Children's Hospital were reviewed and classified as shown in Table I.

From the Los Angeles Children's Hospital.

TABLE I

DISTRIBUTION OF TYPES OF MENINGITIS

TYPE OF MENINGITIS	AGE LIMITS	NUMBER OF CASES
B. tuberculosis	6 mo.-9 yr.	52
Meningococcus	2 mo.-7 yr.	12
Streptococcus (Alpha type)	1 mo.-6 yr.	11
B. influenzae	1 yr.-4 yr.	7
Streptococcus (Beta type)	2 yr.-10 yr.	6
Pneumococcus	2 mo.-2 yr.	4
Streptococcus (not typed)	2 mo.-8 yr.	3
Streptococcus mucosus	7 yr.	1
Staphylococcus (not typed)	2 days	1
B. coli communis	5 mo.	1
B. enteritidis	15 mo.	1
Syphilitic	1 yr.	1

In Table I only those cases of tuberculous meningitis are included in which the organism was demonstrated in smears from the spinal fluid or in which conclusive gross microscopic evidence was present at autopsy. In the other nontuberculous cases the organisms were obtained from spinal fluid cultures during life with the exception of a few instances in which the culture was obtained from the exudate at autopsy. The large number of tuberculosis cases was partly dependent on the large Mexican population in which the disease is particularly prevalent. The relatively small number of meningococcus cases was due to the absence of this disease in epidemic form at the time these cases were observed. Mortality figures in the meningococcus cases are not available, because of the transfer of these patients to the Contagious Division of the Los Angeles General Hospital as soon as the diagnosis was established. Mortality in the remainder of the series was universal, with the single exception of the one syphilitic case.

The one case in this series caused by *Bacillus enteritidis* will be reported in detail.

REPORT OF CASE

History.—L. P., a white female, fifteen months old, entered the hospital on May 31, 1931. Birth and previous history were not unusual. Both parents and an older brother were living and well. The patient had been well until two weeks before when a "head cold" associated with several loose stools daily was noted. Fever, vomiting, and listlessness developed. Three days following the onset of illness, there occurred a general convulsion of one and one-half hours' duration. The child became progressively stuporous, and convulsive seizures were repeated on three occasions.

Physical Examination.—The child was dehydrated and poorly nourished, weighing seventeen pounds. She was stuporous and aroused with difficulty. Marked neck rigidity was present; occasional purposeless fluttering movements of the hands and slight weakness of the left arm and leg, were noted. The pharynx was inflamed. No other abnormalities were observed.

Laboratory Data.—The spinal fluid was cloudy and under increased pressure. Cell counts on various occasions ranged from 500 to 6500 cells per cubic milli-

meter, 98 per cent of which were pus cells. Blood examination showed 38 per cent hemoglobin (Dare) and 2,660,000 erythrocytes. Leucocytes numbered 21,900. A differential count showed: polymorphonuclears, 86 per cent; lymphocytes, 11 per cent; mononuclears, 3 per cent. Urine examination was negative except for a faint trace of albumin. Spinal fluid and blood cultures produced *B. enteritidis* (Gärtner) which was confirmed by cultural and serologic study.

Bacteriological Diagnosis.—Morphology and Staining. Direct smears from the purulent cerebrospinal fluid stained with Gram's method revealed numerous cells, and gram-negative, nonsporiferous rods, mostly extracellular. The differential count was 98 per cent polymorphonuclear cells and 2 per cent lymphocytes. The bacilli proved to be actively motile when some of the fluid was placed on a hanging drop slide.

Cultural Characteristics. The organisms in the spinal fluid grew abundantly in veal broth, on blood agar plates, on bacto-eosin methylene blue agar plates, on bactonutrient agar, and on heart infusion agar slants. The rods measured from 1.69 to 1.81 microns in length and 0.338 micron in width. These measurements were taken after the organisms had been transplanted several times. The surface colonies measured from 1 to 2 mm. in diameter. The colonies were finely granular in structure although they had a smooth appearance. The edges of the colonies were thin while the centers were somewhat dome shaped. There was no hemolysis produced on blood agar plates. In veal broth a pellicle was formed after seventy-two hours of incubation. On veal blood agar the growth was slightly gray in color; on eosin methylene blue agar plates, the colonies were faintly pink; and on bactonutrient agar and heart infusion media the growth was yellow in color and butryous in consistency. Cultures from the spinal fluid obtained at the second and third lumbar punctures produced the same organisms.

A blood culture taken June 6, 1931, produced organisms identical with those found in the spinal fluid after 48 hours' incubation.

Biochemical Reactions.—The organisms produced in culture from the spinal fluid and blood formed acid and gas in a 1 per cent carbohydrate medium of dextrose, mannite, and maltose. Fermentation was not produced in lactose or in saccharose. Indol was negative.

Serologic Reactions.*—Technic of Agglutination Tests. Typhoid, para A and para B antiserums, and enteritidis antiserum, were used in the tests.

TABLE II

RESULTS OF AGGLUTINATION TESTS WITH ORGANISM FROM SPINAL FLUID. ANTIGEN ORGANISM PRODUCED IN SPINAL FLUID

	DILUTIONS OF ANTISERUMS									
Antiserum	1-20	40	80	160	320	640	1,280	2,560	5,120	10,240	20,480
Typhoid	+	+	+	−	−	−	−	−	−		
Para A	−	−	−	−	−	−	−	−	−		
Para B	+	+	+	+	−	−	−	−	−		
Enteritidis	+	+	+	+	+	+	+	+	+	−	−

The antigen was made by washing with sterile normal saline nutrient agar slants of 24-hour cultures from the spinal fluid and blood of the patient. Three drops of 10 per cent formalin was added to the suspension to inhibit growth. One tenth of one cubic centimeter of each of the antiserums was used. After the agglutination tests were prepared, they were shaken well and incubated overnight at 37.5° F. The next morning the tests were placed in the ice box for half an hour before reading.

*The typhoid, para A and para B, antiserums used in the tests were purchased from Parke, Davis & Company. The enteritidis antiserum was obtained from the Los Angeles County Health Department.

TABLE III

RESULTS OF AGGLUTINATION TESTS WITH ORGANISMS OBTAINED BY BLOOD CULTURE. ANTIGEN ORGANISM PRODUCED IN BLOOD CULTURE

	DILUTIONS OF ANTISERUMS										
Antiserum	1-20	40	80	160	320	640	1,280	2,560	5,120	10,240	20,480
Typhoid	+	+	+	−	−	−					
Para A	−	−	−	−	−	−					
Para B	+	+	+	−	−						
Enteritidis	+	+	+	+	+	+	+	+	+	+	−

After the results shown in Table III were obtained, an agglutination test was made using blood serum from the patient, with an antigen made from a known pure culture of *Bacillus enteritidis.*

TABLE IV

RESULTS OF AGGLUTINATION TESTS WITH PATIENT'S BLOOD SERUM. ANTIGEN OF KNOWN PURE CULTURE OF *B. Enteritidis*

	DILUTION OF SERUM									
Serum	1-20	40	80	160	320	640	1,280	2,560	5,120	10,240
Blood serum from patient	+	+	+	+	+	+	+	+	−	−

Because *Bacillus enteritidis* is so rarely found in spinal fluid, a culture was sent to Dr. Karl F. Meyer of the University of California. He reported the organism to be biochemically and serologically typical *Bacillus enteritidis* (Gärtner).

Clinical Course.—Fever was persistent and variable, ranging from 101° F. to 105° F. No diarrhea or abnormal stools were noted. Convulsions were frequent, and the child became progressively weaker until death occurred on June 13, 1931, approximately one month after the onset. Therapy was limited to frequent spinal drainage by lumbar puncture, sedatives, and feeding by gavage.

Autopsy.—Dr. C. M. Hyland performed the examination on the day following death. The brain was swollen, congested, and extensively covered by a purulent exudate. The colon showed occasional small ulcerations of the mucosa. The solitary follicles and mesenteric lymph glands were hyperplastic. The remainder of the intestinal tract was negative. An exudate found in the left mastoid antrum, unsuspected clinically, yielded *Bacillus enteritidis* on culture. Culture from the bowel at autopsy revealed *Bacillus coli communis.*

COMMENT

Thorough study of the organism by cultural and serologic methods leaves no doubt as to the correct classification of the offending organism in this patient. The colitis found at autopsy, with the history of diarrhea preceding the onset of meningeal symptoms, suggests that the portal of entry of infection was the intestinal mucosa. The positive blood culture warrants the assumption that the meningeal involvement was metastatic through the blood stream. The finding of *Bacillus enteritidis* in the mastoid antrum is interesting since the tympanic membranes showed no evidence of middle ear infection during life.

SUMMARY

1. A case of meningitis caused by *Bacillus enteritidis* of *Gärtner* is reported in a fifteen-month-old infant.

2. The bacteriologic characteristics of the organism are discussed, and the incidence of causative organisms is given in a series of 100 cases of meningitis in infants and children.

To Dr. Phillip E. Rothman, at whose suggestion this report was written, I wish to express appreciation of his continued help and interest. I am indebted to Miss Marion R. Anderson for her technical assistance in the bacteriologic study.

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CONVULSIONS IN CHILDREN

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A CONVULSION is a series of involuntary contractions of a group or several groups of muscles usually associated with a loss of consciousness. Initiated by various stimuli, convulsions originate in the motor area of the cortex, which transmits impulses through the brain to the anterior horn cells of the spinal cord and finally to the muscles. This symptom-complex, though occurring during all stages of life, is notoriously frequent in children, the frequency of which is inversely proportional to the age of the child. As the child grows older, the incidence of convulsions gradually decreases so that they are relatively infrequent after six years of life.

Morse[1] explains the frequency of infantile convulsions by the following two factors:

a. In infancy there is a rapid growth of the brain, which makes it more vulnerable and irritable than its slower growing neighbors.

b. The higher cerebral centers, inhibitory in action, are imperfectly developed in infancy and childhood and are thus less able to restrain discharges from lower centers than when perfect development occurs.

That heredity undoubtedly plays some part in the selective action in the development of convulsions offers an explanation for the absence of this symptom-complex in some children and its presence in others. Children born of neurotic parents have a greater tendency to suffer from convulsive attacks than children who have a more stable family background.

The exciting causes of convulsions are five in number, namely: toxic, organic, epileptic, reflex, and metabolic.

1. Toxic.—

a. The onset of acute infectious diseases is often ushered in by convulsions. This usually occurs after the first three years of life.

b. Autointoxication is a very frequent causative factor, especially in children under four years of age.

c. Acute disease of the nervous system causes the severest type of convulsions If convulsions persist in spite of symptomatic treatment, a diagnostic spinal puncture should be made.

d. Toxic convulsions in the newborn, though relatively infrequent, are usually due to the presence of bacterial infections involving the skin, nasopharynx, or umbilicus. A more infrequent cause is the absorption of toxins through the circulation or milk of eclamptic mothers. Lead poisoning caused by a nipple shield or salves on the nipples of the mother is a possible cause. An enlarged thymus (classed as

From the Touro Infirmary.

toxic or reflex) is an infrequent factor. Syphilis is seldom a cause.

2. Organic.—This is the most frequent cause of convulsions in the newborn and is usually manifested within the first month of life.

a. Intracranial hemorrhage, traumatic or due to asphyxia from a prolonged and difficult labor or associated with a hemorrhagic diathesis, is the most common cause. The convulsions may be either clonic or tonic, usually appearing within the first forty-eight hours of life. Between convulsions the patient is drowsy, refuses to nurse, and has a feeble cry and a possible bulging of the fontanel. The spinal fluid shows gross blood or a xanthochromic fluid due to the destruction of the red blood cells. The absence of blood may indicate the presence of hemorrhage within the brain substance.

b. Congenital anomalies are infrequent causes.

3. Idiopathic Epilepsy.—According to Boyer "a seizure to be truly epileptiform must be transient, must impair or cause loss of consciousness and must ultimately result in some change, however slight, in the personality of the patient." This type of convulsion is not accompanied by any visible pathologic features. It occurs most frequently between the ages of five and ten years.

4. Reflex.—This factor is almost negligible, in spite of the large number of cases attributed to teething, worms, phimosis, and foreign bodies in the ear or nose. Teething at the most will cause slight fever, nasopharyngitis, otitis media, anorexia, and some restlessness. An enlarged thymus which may be classed as either toxic or reflex is an infrequent cause.

5. Metabolic.—Spasmophilia or tetany composes the metabolic group. It occurs most frequently in children between eight and thirty-six months of age. Its seasonal incidence is usually from May to June. The calcium content of the blood stream is usually below 7.5 mg., and often 5 mg., per 100 c.c. of blood.

The attacks occur spontaneously when the calcium level is as low as 7 mg. per 100 c.c. of blood.

Latent tetany, the calcium content of which is less than 8.5 mg., is made active when an added impetus is present, as slight toxemias, constipation, etc.

The etiology of convulsions has been variously treated by many writers, most of whom make the general statement that the majority of convulsions in children are based on the presence of a latent tetany.

In forty-five cases of convulsions at Touro Infirmary personally observed or investigated during a five-year period, the frequency of latent tetany is not substantiated.

Of the forty-five cases, eighteen were diagnosed as autointoxication, three epilepsy, five tetany, one cerebrospinal injury, one acute tonsillitis, one syphilis, and sixteen as "convulsions" (no etiological diagnosis).

Calcium and phosphorus determinations permitted a diagnosis of tetany in five, or 11.1 per cent of these cases. Whaley,[14] chemist at Touro Infirmary for the past ten years, states that he has observed only a minor connection between convulsions and latent tetany.

As shown by the clinical picture and laboratory findings in this series, the illnesses were for the most part mild in nature. These are the minor disturbances which are usually classed as the initiators of convulsions in cases of latent tetany.

In this series the calcium and phosphorus determinations are used as the criteria for the diagnosis of tetany although the writer realizes that occasionally true tetany occurs when the calcium is normal. In such cases there is a negative calcium balance in which more calcium is excreted than consumed. The importance of this is negligible because of its infrequency.

The normal calcium is assumed to be from 9 to 11 mg. per 100 c.c. blood, this being based on the findings of Trumper and Cantarow[2] and Englebach.[3] The normal phosphorus level in children is from 4 to 6 mg. per 100 c.c. of blood. A calcium level of 8.5 mg. or less is assumed as a basis for a diagnosis of tetany.

TABLE I

	NUMBER OF CASES	AVERAGE W.B.C.	DIFFERENTIAL	AVERAGE TEMPERATURE	AVERAGE CALCIUM	AVERAGE PHOSPHORUS	NUMBER POSITIVE WASSERMANN	AVERAGE AGE
1. Autointoxication	18	9,300	N60 L39 E 1	102°	10.8 – 5.5		1	3 yr.
2. Epilepsy	3	13,000	N61 L39	98°	11.1 – 5.3		0	5 yr.
3. Tetany	5	10,000	N50 L48 E 2	100°	7.7 – 3.8		0	2 yr.
4. Cerebrospinal injury	1	15,000	N20 L80	98°	9.0 – 5.9		0	1½ mo.
5. Acute tonsillitis	1	10,500	N70 L30	104°	11.1 – 5.2		0	8 mo.
6. Convulsions	16	11,000	N53 L44 E 3	102°	10.8 – 5.0		0	4½ yr.
7. Syphilis	1	6,000	N69 L31	98°	10.0 – 4.9		1	4 yr.

It is generally agreed that tetany is intimately associated with rickets. Consequently there is a tendency to diagnose as latent tetany most of the cases of convulsions in which there are signs of rickets.

Trumper and Cantarow[2] stress the fact that in the great majority of cases of rickets the serum calcium is within normal limits, the most prominent feature being a decrease in the level of the serum phosphate. In some instances, however, hypocalcemia occurs with manifestations of tetany.

Thus it is seen that while tetany is almost always associated with rickets, rickets is infrequently associated with a low serum calcium and, consequently, tetany. On this basis the careless diagnosis of latent tetany based on the presence of rickets should be largely disregarded.

The damage sustained by the central nervous system as a result of convulsions is an important consideration in the light of clinical investigation. The time-honored statement of many pediatricians and general practitioners that convulsions in children need not be considered seriously is unwarranted, as there seems to be a relation between infantile convulsions and brain damage. But it must be borne in mind that the convulsion may be a symptom of a damaged nervous system or that the convulsion may have produced the damage.

In a series of 265 unselected cases with a history of infantile convulsions Thom[4] found 29 per cent to be mentally deficient or epileptic. Still[5] has pointed out that a comparatively small number of the individuals who have convulsions ever become epileptic. On the other hand Osler[6] found that 40 per cent of the cases under his observation which were diagnosed as epileptic gave a history of infantile convulsions.

General statistics compiled by neurologists show that 22 per cent of the cases of infantile convulsions later develop epilepsy as compared to the pediatricians' statistics showing 7 per cent.

One case observed by the writer stresses the prime importance of convulsions as related to brain damage, and consequently the future welfare of the individual. This patient, aged nine months, had a severe attack of convulsions lasting about one hour; they were caused apparently by intestinal influenza. Twenty-four hours later a spastic hemiplegia developed. After a week a partial return of activity occurred. At the present time six months have elapsed with a complete return to normality as far as can be observed. What the mental capacity in the future will be is yet to be determined. In this case an evident cerebral hemorrhage occurred. One can only surmise the frequency of minute, unrecognizable hemorrhages sustained in convulsions. In the light of such findings infantile convulsions should be looked upon more seriously and a greater effort be made to prevent their occurrence during early life. In this way much epilepsy and mental deficiency will be prevented.

The treatment of convulsions should aim toward an early dissolution of the symptoms for the sake of the welfare of the child and the relief of the mental strain of the family. The first part of the treatment consists of a cold bath when fever is present or a warm bath when the temperature is normal. This is then followed by a high enema.

If relief is not obtained at once, the free use of drugs should be instituted, namely: morphine, chloral hydrate, sodium bromide or luminal. Chloral hydrate in combination with the bromide is well tolerated by infants; no hesitancy should be felt in repeating the dose as often as necessary. The combination of chloral hydrate and bromide is best administered by rectum. If good results are not obtained in a short time, the use of chloroform or ether is strongly recommended. The fact that the longer the convulsion lasts, the greater is the chance of damage to the nervous system, should be borne in mind.

Continuous muscle twitching not relieved by the above-mentioned treatment is an indication for a spinal puncture. This is of more diagnostic than therapeutic use.

As soon as possible, a purgative should be then given the patient. After complete relief of the symptoms, a diagnosis should be made and treatment instituted. Cases with doubtful etiology should be given the benefit of detailed laboratory investigation. In this way vague conditions may be relieved thus preventing future attacks of convulsions with subsequent mental deterioration and epilepsy.

CONCLUSIONS

1. The exciting causes of convulsions are five in number, namely: toxic, organic, epileptic, reflex, and metabolic.

2. Latent tetany is an infrequent cause of convulsions.

3. In forty-five cases of convulsions tetany was present in five, or 11.1 per cent.

4. A diagnosis of tetany or latent tetany should be made only when there is less than 8.5 mg. of calcium per 100 c.c. of blood.

5. Convulsions as a possible cause of epilepsy and mental deterioration are to be stressed.

6. Immediate control of convulsions is necessary to decrease the incidence of damage to the nervous system.

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ESOPHAGEAL VARIX

Report of Case in a Three-and-One-Half-Year-Old Child, Not Dependent on Liver Cirrhosis

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RELATIVELY little space is devoted in textbooks on medicine and pediatrics to the discussion of varix of the esophagus as a clinical entity. Indeed, this subject is considered by Finkelstein,[1] Feer,[2] Holt,[3] Garrod, Batten, and Thursfield,[4] Tice[5] and Blumer[6] only indirectly as a possible source of bleeding in hepatic cirrhosis, Banti's disease, and related conditions. Abt,[7] Anders and Boston,[8] and Mathe[9] dismiss the subject with the utmost brevity. Cecil[10] is somewhat more generous, allowing eleven lines to its consideration. The impression that it is especially infrequent during childhood finds confirmation by failure to discover a single reference to the subject in the pediatric yearbooks from 1919 to 1932. The *Index Medicus* for 1931 contains only five references, three in German and two in American literature. It is, therefore, deemed worth while to report the following case which may be regarded all the more unusual because it is not dependent for its genesis upon hepatic cirrhosis. A summary of the various aspects of this subject, based upon a survey of the literature, is appended.

CASE REPORT

R. L., male, three and one-half years old, was admitted to the Children's Hospital, November 27, 1932, because of hemorrhage from the stomach and intestines.

The family history was irrelevant.

The patient had had measles, whooping cough, and mumps during the second year of life. His general health had been considered good.

His present illness began when he was eighteen months old with nausea followed by vomiting of a large amount of bright red blood. Shortly thereafter tarry stools appeared. He seemed quite well for about one year when there was a recurrence of bleeding. Three months later he sustained a third hemorrhage. Bleeding again occurred on Thanksgiving Day. Recovery from hemorrhage usually took place in from two to seven days. Fever accompanied each hemorrhagic episode and occasionally reached 104° F. At times mild abdominal pains were noted. His stools were habitually frequent, eight to ten times daily, and, during the intervals between bleeding, presented a normal appearance.

Physical examination disclosed a pale, normally developed, poorly nourished cooperative child, who appeared moderately, but not alarmingly ill. Respirations were somewhat embarrassed by obstruction incidental to an acute upper respiratory infection. The posterior cervical glands were slightly enlarged. The lungs were negative; the cardiac area was normal; heart rate increased; and a systolic murmur was audible. The abdomen was distended, but not tender. The spleen

appeared enlarged, particularly upon percussion. The liver showed no hypertrophy. There was a large right inguinal hernia present. In other respects, the examination was negative.

The admission diagnosis made by the resident, Dr. F. Bender, was varices in lower esophagus or possible ulcer of stomach.

Laboratory findings.—The urine presented no abnormality. The stools were distinctly tarry. Hemoglobin, 58 per cent; erythrocytes, 3,300,000; leucocytes, 6,000. Polynuclears, 65 per cent; lymphocytes, 31 per cent; large mononuclears, 4 per cent; blood platelets, 180,000; bleeding time, fifteen seconds; and coagulation time, four minutes. Hemolysis began at 0.38 per cent and was complete at 0.32 per cent. The Wassermann test was negative.

Further observation.—Nov. 28: The child was playful, ate with evident relish; sleep was undisturbed; temperature, 99° F. Nov. 29 to Dec. 2: Condition was unchanged; stools were black and semiliquid, numbering from three to four a day; temperature 100°-104° F.; the rise was attributed to the upper respiratory infection; pulse from 120 to 130, and respirations from 24 to 30. Dec. 3: Appetite was good; he had three bowel movements containing well-formed particles. He was given a transfusion of 120 c.c. of uncitrated blood with no immediate unfavorable effects. Dec. 4: The patient slept undisturbed until 2 A.M. when he evacuated a large amount of bright red blood, followed in rapid sequence by three smaller bloody passages. His pulse became exceedingly rapid, almost imperceptible and respirations hurried and superficial. In spite of every effort to check the bleeding and bolster up a failing heart, the patient expired at 8 A.M.

Treatment had consisted of therapy for the upper respiratory infection, a bland diet, transfusion, and upon the advent of the fatal hemorrhage, of coagulants, glucose under the skin, and sedatives to control restlessness.

Autopsy, performed by Dr. E. I. Dobos, director of pathology, revealed the following conditions. The heart and lungs were negative. The esophagus was the seat of extremely large venous plexuses, with occasional hemorrhagic areas in its lower aspect. The cardiac orifice of the stomach showed several small mucosal ulcerations. The stomach contained one large clot estimated to represent 8 ounces of blood, and the intestines contained perhaps a like amount of clotted blood. No dilated veins were found in stomach or bowel, and these organs presented no pathology other than a striking anemia, which likewise characterized all the viscera. The spleen and liver were not enlarged.

DISCUSSION

The provisional diagnosis advanced by the admitting physician was varix of the esophagus or a gastric ulcer. Hemophilia and purpura were considered and readily excluded. Banti's disease was deemed unlikely because of a decided proneness to its occurrence in later childhood. Ulceration of a Meckel's diverticulum could not conceivably account for the hematemesis. Gaucher's disease was untenable because of a negative family history and absence of striking splenic enlargement. X-ray investigation was requested but deemed inadvisable by the roentgenologist because of bleeding. Esophagoscopy was contemplated upon subsidence of the respiratory infection.

HISTORICAL

Varicose dilatation of the esophagus was first observed by le Diberder and Fauvel in 1838 and reported twenty years later.[11] Their patients

were two adults with cirrhosis who died from hemorrhage due to rupture of an esophageal varix. The few case reports which appeared in foreign journals up to 1880 ascribed the condition to alcoholic cirrhosis. In 1880 Le Due[12] encountered a case of syphilitic origin. The first case placed on record in the American literature is that of Van Bibber in 1887, in which the diagnosis was reached at necropsy. In 1897[12] an editorial in the *Medical Record* stressed the importance of varicosity of the esophagus as a source of hematemesis and melena—occurrences almost exclusively identified at that period with gastric and duodenal ulcers.

PATHOGENESIS

The association of portal cirrhosis with esophageal varix was emphasized even by the older observers, and today cirrhosis is recognized as the predominant cause of this esophageal anomaly, which in turn is regarded as one of the commoner causes of hematemesis. Preble[13] in 1900 reported sixty cases of fatal gastrointestinal hemorrhage and in 80 per cent of these, varices of the esophagus were found. Of 126 patients with portal cirrhosis collected by Blumenau in 1920, 19 per cent succumbed to vascular lesions, principally varices of the esophagus. More recently (1929) Mc Indol[13] reported twenty-six deaths due to portal cirrhosis, and in 50 per cent of these the immediate cause was a ruptured esophageal varix. That esophageal varices may occur without concomitant cirrhosis is made evident by the researches of Nochimowski[11] who succeeded in collecting eight cases from the literature, to which he adds two cases from personal observation. Each one of these ten patients succumbed to hemorrhage from rupture of a varix. The series comprises six male and one female adults, and three children, respectively three days, six years, and eleven years old. Congenital weakness of the walls of the veins is probably a predisposing factor in the evolution of the varices in these cases. In the opinion of some, the removal of the spleen may, years later, eventuate in the development of esophageal varix. This belief is especially prevalent among Italian observers. Mathe[10] presents details of one such case.

INCIDENCE

The condition is more frequent than the scarcity of case reports would lead one to believe. It is Preble's opinion that routine injection of esophageal veins in the course of autopsies would reveal many unsuspected cases. Rossle[11] states that from 7 to 8 per cent of deaths from cirrhosis are directly due to bleeding from an esophageal varix. French and German surgeons and pathologists are more keenly alive to the possibility of its occurrence than our American colleagues. Its highest incidence is reached at the age of from 35 to 40 years. However, it occurs

in infancy and in childhood, as well as in the aged. In adult life, the male is more often affected than the female.

ANATOMICAL FINDINGS

The esophagus presents a fine network of veins especially in its lower aspect. This drains chiefly into the coronary gastric vein which in turn empties into the portal vein directly or into the splenic vein near its junction with the portal vein. With the occurrence of portal obstruction[13] "the comparative directness of the communication of the portal and caval systems through the esophageal veins no doubt favors this over others as an anastomotic pathway. Lack of support of the submucosal tissue and the aspirating effect of the negative intrathoracic pressure with respiration and the incompetence of the valves in adult life are responsible factors."

SYMPTOMATOLOGY

Dilatation of esophageal veins may remain symptomless over a period of years. The most striking symptom is a sharp sudden vomiting of blood. The first hemorrhage, if massive, may prove fatal. More frequently hemorrhage recurs at intervals of weeks or months. Hematemesis may be preceded by coughing and a tickling sensation in the throat for about two weeks, which cease with the onset of bleeding. Hemorrhage may occur while at rest, or even during sleep, or following exercise. It may be precipitated by sharp particles of food or by use of the stomach tube. If loss of blood is extensive, a state of shock may supervene. If bleeding is repeated at short intervals, anemia or icterus may result, with loss in weight and strength. During active bleeding, fever is frequently noted. Gastric symptoms, including pain, are conspicuously absent. Blood in the stools, unaltered, or tarry in character, is almost invariably found. General dilatation of the venous system, especially involving the veins of the legs, scrotum and rectum, may coexist. Nochimowski[11] encountered two cases of this description. The endoscopic findings are graphically described by Gordin:[12] "Varices are most abundant at the lower third of the esophagus and at the cardiac orifice. They appear as irregular, tortuous and rounded nodular elevations on the surface of the folds of the esophagus, dark blue in color, easily compressible, strikingly like a clump of small hemorrhoids. The less advanced varices are seen as dilated bluish vessels having a sinuous course, close under the mucosa, through which they stand out vividly. Erosions may occur on the surface of the varices. A great amount of bleeding may occur from erosions of small size." In some the dilated veins reach the size of a lead pencil. However, the bleeding site cannot always be found. Nochimowski believes that when the condition is associated with cirrhosis, the esophagus is involved throughout its extent; and in the absence of ac-

companying cirrhosis, only the lower third is implicated. Operation discloses the stomach and bowels filled with altered or with fresh blood. These organs disclose no pathologic changes.

POSTMORTEM FINDINGS

Autopsy may reveal in addition to dilated esophageal veins, hepatic cirrhosis and splenomegaly and less frequently cardiac and renal pathology. Dilatation of the veins of the legs, scrotum and rectum may coexist. In the presence of marked splenomegaly, portal congestion and congestion of its tributaries are found. The affected veins may be found completely collapsed at autopsy, even if these showed marked dilatation during life; thus the condition may readily escape detection. The point of rupture may likewise be quite inconspicuous. However, injection with air or fluid will render it strikingly prominent. This procedure should be carried out in doubtful cases.

DIAGNOSIS

A diagnosis of bleeding esophageal varix is all too often made only at autopsy. The usual diagnosis is gastric or duodenal ulcer. A painstaking history and a complete blood study added to a comprehensive physical survey will help exclude such causes of hematemesis or melena as carcinoma, leucemia, agranulocytosis, vicarious menstruation, rupture of aortic aneurysm into stomach, nasal or nasopharyngeal bleedings, and in infancy or childhood particularly, the hemorrhagic condition of the newborn sepsis thrombopenic purpura, hemophilia and a possible ulcer of Meckel's diverticulum. Gastric hemorrhage in association with enlargement of liver and spleen should be regarded as presumptive of a ruptured esophageal varix. Jolasse[11] reminds us that in young children and in males past forty, gastric hemorrhage has its most frequent inception in esophageal varices; whereas in the third and fourth decades, peptic ulcer is the chief cause. Diagnosis may be assisted by the x-ray[14] following a barium meal. This will disclose marginal defects of the esophagus, permanent in situation, and rounded or polypoid in outline. Chevalier Jackson and his associates and Wolf (1928) find the roentgenogram distinctly helpful, whereas Cecil[10] and others have failed to derive diagnostic aid from this source. The esophagoscope constitutes indisputably the most certain means of reaching a diagnosis.[13] Cecil admonishes against endoscopic or even roentgenologic investigation during active bleeding. Others,[13] however, show no fear or hesitancy of utilizing these diagnostic agents even in the presence of active bleeding.

PROGNOSIS

Because of the frequent association of advanced cirrhosis, the prognosis in older patients is usually not promising. It is somewhat more favorable in the young because this causative factor is less frequently

operative. Stephan[15] was successful in saving his three-and-one-half-day-old patient by means of energetic therapy, and Peiper[15] met with equally gratifying results in connection with his two patients.

MANAGEMENT

Conditions that are known to lead to the development of liver cirrhosis should be corrected. Active bleeding is an indication for complete mental and physical rest and a liquid diet. Bismuth subnitrate taken slowly with a minimum amount of water may be of help. Stephan obtained satisfactory results by the subcutaneous or intramuscular injection of gelatin supplemented by its use by mouth. Bland tepid food thoroughly masticated, taken in small boluses, in the experience of Kirklin, Moersch, and others[14] tends to prevent traumatization of the thin-walled varices. Avoidance of undue physical exertion should be stressed. In far-advanced cases, the Talma-Morison operation whereby adhesions are established between various abdominal organs and the abdominal wall, resulting in the development of new anastomotic vessels, is advocated. Walters[16] divides the coronary veins and their branches in order to interrupt the flow of blood into the esophageal veins. Splenectomy is advocated by some as a means of relieving an engorged portal circulation. In the experience of Moyer and others this operation failed to check bleeding due to varix of the esophagus.

SUMMARY

This case report represents the unusual picture of idiopathic varix of the esophagus in a male child three and one-half years old. Only ten cases have thus far been reported in which the condition was not dependent upon hepatic cirrhosis. Two of these occurred in the newborn, and one in childhood. The symptomatology and course pursued in the case herein presented conformed closely with the observations of the reported cases. The striking features were recurrent gastric and intestinal hemorrhage extending over a period of one and one-half years, moderate weakness and anemia, absence of pain and gastric symptoms, febrile reaction during the stage of active bleeding, and death as a result of massive hemorrhage. A noteworthy departure was the frequency of stools over a period of several months. The true nature of the bleeding was suspected upon admission. Autopsy revealed prominent dilatation of the veins of the esophagus and ruptured esophageal varix. Neither the stomach nor the intestines showed any abnormality. Enlargement of the spleen and cirrhosis of the liver were not found.

COMMENT

Varix of the esophagus is of more common occurrence than is suspected from the scarcity of case reports. It should be thought of in all instances of bleeding from the gastrointestinal tract, particularly if splenic

or hepatic enlargement coexists. It may occur at any age. During childhood it is usually due to congenital weakness of the veins of the esophagus. In later life, it is usually dependent upon hepatic or splenic pathology. The ultimate prognosis is poor, death usually occurring from loss of blood due to rupture of a varix. All types of treatment proposed have proved unsatisfactory.

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326 Republic Building

HYPOTHYROIDISM AND CRETINISM IN CHILDHOOD

II. Capillary Permeability

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IT SEEMED desirable to examine the permeability of capillaries in a varied group of children for the purpose of comparison with our hypothyroid group.[1] To carry out this study we adopted the use of a cantharides blister, which Petersen[2] and Gänsslen[6] have devised as a simple means of studying capillary permeability by determining the ratio of protein that comes into the blister when compared with the protein concentration of the blood serum.

METHOD[3]

Blisters were produced by a cantharides plaster placed in the middle of the inner surface of the forearm in the older children and between the scapulae in infants. They were applied at definite times (6-8 A.M. for ambulatory patients, 9-10 A.M. for hospital patients). In infants the area of application was observed at intervals for evidence of blister formation. The time when the first definite elevation appears has been taken as the blister time. In older children, an itching sensation commonly brings the plaster to the attention of the patient and in these instances the blister usually showed evidence of formation. The blister was evacuated soon after its appearance.

The refraction index of solutions is proportional to their protein content. The content of the latter in the blister fluid and in the blood serum is ascertained by determining their refraction indices. The readings for the serum are made according to the regular serum table, those for the blister fluid from the Reiss exudate table.

The factors underlying alterations in capillary permeability have been adequately discussed in a group of articles.[3, 4]

The blister time is the period between the placement of the blister and the first evidence of its presence.

1. The permeability ratio is the

$$\frac{\text{percentage of blister protein}}{\text{percentage of serum protein}}$$

This coefficient indicates the actual degree of response of the capillary endothelium to a direct stimulus.

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We wish to express our appreciation to Dr. W. H. Petersen for his aid in this study.

2. The inflammatory index is the

$$\frac{\text{permeability ratio}}{\text{blister time}}$$

This coefficient reveals the effect of the autonomic tonus.

NONHYPOTHYROID GROUP; ANALYSIS OF RESULTS

Blisters were applied to forty-five hospitalized children (four of the group being colored) during the months of May and June, 1932. The diagnosis in each is listed in the table. The children ranged in age from two months to thirteen years, eight were one year and under, twenty-five were under eight years, and twelve over eight, the oldest being thirteen. There were twenty female children and twenty-five males.

The average time for blister formation was 5.4 hours, the lowest time for production was 3 hours and the longest period 8 hours. In thirty-five of the patients it took 5 hours or less for the appearance of the blister. In ten children it took over 5 hours, being apportioned as follows: in two, 6 hours; in one, 6.5 hours; in five, 7 hours, and in two, 8 hours.

The average permeability was 66.6, the highest being 83 and the lowest 43. In twenty-three children the permeability was above 66.6 and in twenty-one below.

The average inflammatory index was 13.85 per cent, the highest being 26.7 and the lowest 5.37. In thirty-seven of the forty-five patients this index fell between 10 and 17 per cent.

In this group of nonhypothyroid children, blister determinations indicate that decreased permeability may be associated with increased blister time and increased capillary permeability may run along with decreased blister time. No reciprocal relationship exists between the degree of permeability and the length of blister time.

HYPOTHYROID GROUP

The hypothyroid patients studied were those discussed in the first paper of this series.[1] Petersen[2] studied the effect of hormones in a small series of goiter cases and demonstrated that increased thyroid secretion increased capillary permeability. Gellhorn and Northup[5] in perfusion experiments on animals found that thyroxin increased the permeability of the gut membrane. Gänsslen[6] in his studies found a short blister time in hyperthyroidism and a prolonged blister time in hypothyroidism and myxedema.

ANALYSIS OF RESULTS

Blisters were applied at intervals to eleven children with thyroid deficiency over a period of several months. These patients ranged in age from four months to fifteen and one-half years. There were eight males and three females. The average time for blister formation in the

hypothyroid children when receiving thyroid medication was usually within the average time as determined in the group of nonhypothyroid children, namely, 5.4 hours.

The permeability and inflammatory indices in the cretins taking thyroid extract were variable. The relation between these indices and the time necessary for the formation of a blister is similar to that found in the nonhypothyroid patients listed in Table I.

TABLE I

GROUP OF 45 NONHYPOTHYROID CHILDREN ARRANGED ACCORDING TO AGE

	AGE	DIAGNOSIS	BLISTER TIME HOURS	BLOOD PROTEIN	BLISTER PROTEIN	PERMEABILITY	INFLAMMATORY INDEX
1	2 Mo.	Normal	3.0	6.06	4.87	80	26.7
2	2½ Mo.	Normal	5.5	5.19	3.17	61	11.0
3	2½ Mo.	Normal	5.0	5.83	3.01	52	10.4
4	3 Mo.	Pylorospasm	5.0	5.37	3.51	65	13.0
5	5 Mo.	Normal	3.5	6.64	3.78	57	16.3
6	9 Mo.	Upper respiratory infection	3.5	7.00	4.49	64	18.3
7	11 Mo.	Cleft palate	5.0	5.89	4.21	72	14.4
8	1 Yr.	Normal	4.5	7.11	4.49	63	14.0
9	13 Mo.	Pyelitis	5.0	8.15	5.10	63	12.6
10	13 Mo.	Achondroplastic dwarf	7.0	6.52	4.05	62	8.8
11	14 Mo.	Cleft palate	4.5	6.12	4.49	73	16.0
12	15 Mo.	Syphilis, malnutrition	4.0	6.76	3.01	44	11.0
13	17 Mo.	Cleft palate	5.5	7.00	5.80	83	15.0
14	21 Mo.	Cleft palate	4.0	7.52	4.16	55	13.7
15	2 Yr.	Tuberculosis	7.0	4.73	2.46	52	7.4
16	2½ Yr.	Feeble mindedness	4.5	7.87	4.70	60	17.0
17	2½ Yr.	Cleft palate	3.5	7.57	4.54	60	13.3
18	3 Yr.	Idiot	5.0	5.37	3.83	71	14.2
19	3½ Yr.	Mongol	6.0	5.89	3.56	60	10.0
20	4 Yr.	Feeble mindedness	4.0	6.94	4.82	69	17.2
21	4 Yr.	Idiot	5.0	7.40	5.04	68	13.6
22	4 Yr.	Eye case	5.0	6.34	4.87	77	15.4
23	4 Yr.	Old palate	8.0	7.46	3.17	43	5.37
24	5 Yr.	Eye case	4.0	7.69	4.21	55	13.7
25	5 Yr.	Eye case	5.0	6.34	4.87	77	15.4
26	5 Yr.	Cleft palate	5.0	7.52	5.47	73	14.6
27	5 Yr.	Tonsillitis	4.0	8.85	5.85	66	16.5
28	5½ Yr.	Rheumatic endocarditis	5.0	7.57	5.42	72	14.4
29	5½ Yr.	Chorea	7.0	7.40	5.10	69	9.8
30	6 Yr.	Herniotomy	8.0	7.00	5.63	80	10.0
31	6½ Yr.	Tonsillectomy	6.5	6.23	4.62	74	11.4
32	7 Yr.	Bronchiectasis	6.0	7.00	4.70	67	11.0
33	7 Yr.	Sister of cretin; normal	6.0	6.40	4.11	64	10.7
34	8 Yr.	Abscess chest wall, tuberculosis	7.0	7.17	5.85	82	11.7
35	9 Yr.	Chorea	4.0	7.75	4.49	58	14.0
36	9 Yr.	Observation for headaches	4.5	Broke			
37	9 Yr.	Cleft palate	4.5	7.34	5.04	68	15.0
38	10 Yr.	Empyema	5.0	7.46	5.58	74	14.8
39	10 Yr.	Eye case		6.87	4.59	66	9.4
40	11 Yr.	Eye case	4.0	7.05	4.87	69	17.5
41	11 Yr.	Endocarditis	5.0	6.12	4.43	72	14.4
42	11 Yr.	Mental deficiency	5.0	5.49	4.43	81	16.2
43	11 Yr.	Obesity	4.5	7.57	5.90	78	17.3
44	12 Yr.	Brother of cretin; normal	3.5	6.00	3.72	62	17.7
45	13 Yr.	Mongolian	4.5	6.32	5.15	75	16.6

TABLE II

HYPOTHYROID GROUP

	DATE 1932	AGE	DIAGNOSIS	BLISTER TIME HOURS	SERUM PROTEIN	BLISTER PROTEIN	PERME-ABILITY	INFLAM-MATORY INDEX	REMARKS
1	June 21	12 Yr.	Cretin	5.0	6.52	3.83	58.0	11.6	Doing very well; no troubles on 2 gr. thyroid extract per day (ambulatory).
2	Feb. 25	15.5 Yr.	Cretin	?	5.71	4.05	71.0	?	1 gr. thyroid extract per day (ambulatory).
3	July 25	14 Yr.	Cretin	None in 7 hr.					3 gr. thyroid extract per day (ambulatory).
4	Apr. 28	7.5 Yr.	Cretin	3.5	7.00	5.63	80.0	23.0	2½ gr. thyroid extract per day (ambulatory).
	June 23			5.0	7.52	5.74	76.0	15.0	
5	Nov. 21	4 Mo.	Cretin	12.0	9.32	5.47	58.0	4.8	Note unusually high protein; no thyroid (ambulatory).
	Nov. 28			12.0	9.32	5.95	63.0	5.25	
6	Apr. 19	4.5 Mo.	Cretin	5.0	7.63	8.78	115?	23.0	½ gr. thyroid extract per day.
	June 2	6.5 Mo.		5.0	5.25	4.00	76 2	15.5	½ gr. thyroid extract per day.
	July 7	7 Mo.		3.5	6.72	5.04	75.0	21.3	No thyroid extract for 2 weeks (hospital).
7	May 13	9 Yr.		No Blister					Off thyroid extract 1 month.
	June 11								Off thyroid extract 2 months (ambulatory).
	Dec. 30	9.5 Yr.		8.5	5.01	3.61	72.0	8.47	On 2-3 gr. thyroid extract per day for 5-6 months.
8	Feb. 17	3.5 Yr.	Cretin	5.0	6.52	5.10	78.0	15.6	No thyroid extract since 1/17/32.
									Insulin 6-8 units since 2/27.
	Mar. 2			6.5	7.00	4.43	63.0	9.7	Insulin 6-8 units since 2/2.
	Mar. 19			5.0	8.33	6.40	77.0	15.4	1 mgm. thyroxin 2/2/32.
				6.0	8.15	6.18	76.0	12.66	
	Mar. 31	4 Yr.		5.0	8.09	5.21	64 0	12.8	
	Apr. 11			4.0	7.57	5.63	74.0	18.5	1½ mgm. thyroxin intravenously.
	Apr. 19			4.0	6.12	4.05	66.0	16.5	
	July 8			5.0	8.04	5.15	64.0	12.8	Thyroid extract 2-2½ gr. per day.

Withdrawing thyroid extract in these patients who have been receiving this medication results either in an increase in the time or an inability to form a blister. This is illustrated in patients 7, 9, and 10.

G. M. (No. 7) had been off thyroid for one month prior to his blister of May 13, and for two months previous to the blister of June 11, 1932. Blisters did not appear. Associated with the failure to raise a blister were a fall in the basal metabolic and pulse rates, and a gain in weight.

J. F. (No. 9) on February 16, 1932, while receiving 2 grains of thyroid extract per day, raised a blister in three hours. The permeability and inflammatory indices were both unusually low. On April 30, he was not able to raise a blister, having been off thyroid medication for two weeks previous to this date and having been on reduced dosage of thyroid extract during the time he had chickenpox. On May 27 after resumption of thyroid medication, a blister appeared in six hours, the permeability ratio was 74, and the inflammatory index, 12.33. On June 23 he entered the hospital for further study. He had been on from 2 to 3 grains thyroid extract per day. Thyroid medication was stopped; the time for formation of blister rose, and the permeability changed to decreased levels, but the inflammatory index definitely fell. After resumption of thyroid medication the blister time fell, permeability again changed but little, and the inflammatory index rose.

O. K. (No. 10) was admitted to the hospital on June 20, 1932, having been on from 2 to 3 grains thyroid a day at home. This preparation was given very irregularly by the parents. After being off thyroid for a short period, the time for blister formation rose, but with the resumption of thyroid medication the results were too varied to allow the drawing of conclusions.

Patients Nos. 5 and 11 are female cretins who never received thyroid. D. B. (No. 5), four months old, was unable to raise a blister under twelve hours. The permeability readings were 58 and 63, and the inflammatory indices were 4.8 and 5.25.

R. P. (No. 11), aged four and one-half years, had six plasters applied from September 9 to 21, and no blisters appeared at any time. Because her tongue was large, and since she vomited so readily, thyroxine was administered intravenously. On September 19, 1932, ½ mgm. thyroxine was given, and on September 23 she raised a small blister, the time not being known; the permeability was 77 per cent. On September 26 after having received a second dose of thyroxine intravenously she raised another small blister, the time not being obtained; the permeability was 89 per cent. From then on she was able to raise a blister usually within five hours. After a time blisters formed so rapidly that before blister fluid could be obtained they had broken. It is interesting to note that on November 7, because of a severe upper respiratory infection, thyroid medication was stopped and not resumed again until November 23. During this period she raised blisters within the five-hour period.

SUMMARY

1. Capillary permeability by means of the cantharides plaster was studied in a group of forty-five nonhypothyroid and eleven thyroid deficient children.

2. In the nonhypothyroid group a single application of the plaster was made. The average time for blister formation was determined as 5.4 hours, twenty-nine falling within the range of 4 to 5 hours.

3. In the eleven hypothyroid children several applications were made in each patient, and in one instance as many as twenty-six.

4. Three of the nine children receiving thyroid were removed from this medication.

(a) One of these was unable to raise a blister.

(b) In two the time for blister formation rose considerably.

5. Of two female cretins who never received medication, one was unable to raise a blister under 12 hours and the other, not until thyroid therapy was instituted.

6. The absence of reciprocal relationship between the time of formation of blisters and the degree of permeability is indicated in the nonhypothyroid group.

7. The variability of the permeability and the inflammatory indices in the thyroid deficient children and the relation between these and the blister time is similar to that found in the nonhypothyroid group.

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THE EFFECT OF COOKING ON THE DIGESTIBILITY OF CEREALS

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IN THESE experiments we have determined the effect of cooking on the digestibility of the starches of various cereals. In the past the consensus of opinion has favoured a comparatively long period of cooking. Recently, however, there is a tendency to question the necessity of such long cooking periods in preparing cereals for the diet of the average child.

A number of feeding experiments have been done with human subjects to determine the coefficient of digestibility or the percentage of the total carbohydrate of the various cereals which is digested and absorbed.[1, 2, 3, 4, 5, 6] These experiments show that during the period of digestion in the human subject practically all (90 per cent to 98 per cent) of the carbohydrate of cereals is utilized, but they do not indicate the ease of digestibility; that is, whether complete digestion occurs more rapidly with one cereal than with another, or what influence the time of cooking may have on the digestibility.

Experiments on the digestibility of cereals have recently been reported by Noble, Dean, Wing and Halliday.[7] These in vitro experiments indicate that digestion is as complete after twenty minutes of cooking as after ninety minutes of cooking.

The process of starch digestion in the animal body may be described as the hydrolytic breakdown of the complex starch molecule to the simple sugar, glucose. The intermediate products in the hydrolysis are soluble starch, dextrins, and maltose. The principal enzyme involved is pancreatic amylase, with ptyalin and finally maltase also taking part in the hydrolysis. From 30 to 76 per cent of the food cellulose is also digested, but this is accomplished by the intestinal bacteria, as none of the enzymes in the higher animals are capable of splitting cellulose.[8]

METHOD

In the following experiments the amount of maltose formed in a given time under standard conditions was taken as the measure of starch digestibility. The amount of maltose formed by digestion was obtained by subtracting from the total amount formed in a sample which had been cooked and then digested, the

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amount found in an aliquot sample which had been cooked for the same length of time and treated in exactly the same manner, except that the digestive enzyme was destroyed immediately before any digestion had taken place.

To judge the effect of cooking on starch digestibility in a given time the following periods of cooking were selected: 0, 5, 15 and 30 minutes, 1, 2, and 4 hours.

One-gram samples of the dry cereal were weighed into each of seven pairs of 125 c.c. Erlenmeyer flasks, 15 c.c. of water was added to each and the flasks placed in boiling water for the desired length of time. The flasks were loosely stoppered and were agitated during the early stages of cooking in order to eliminate clumping and skin formation, both of which, according to other investigators,[9,10] result in retarded digestion. Observations of the temperature within the cooking flasks showed a rapid rise to 95° C. during the first five minutes of cooking. The maximum temperature observed was 98° C.

After removal from the water-bath 10 c.c. of water was added, making a total of 25 c.c. Uncooked samples were allowed to stand in water at room temperature for one hour to ensure saturation of the cereal with water before digestion.

To all the flasks were then added 10 c.c. of 0.2 M. dihydrogen phosphate buffer P_H 6.8, 1 c.c. of 0.2 N. NaCl, and 1. c.c. of enzyme solution, which was a 1 per cent solution of desiccated pancreas in 1 per cent sodium bicarbonate. This solution should be prepared fresh each day. It contains adequate amounts of the starch splitting enzyme, amylase.

The enzyme action in one of each pair of flasks was stopped immediately with 3 c.c. of 3 N.H_2SO_4. The others were incubated and digestion allowed to proceed for exactly thirty minutes in a water-bath at 37° C. The enzyme action was then stopped in this group by the addition of the same amount of acid. At this point the total volume of liquid was 40 c.c. All calculations were based on this volume. After centrifugalization lasting ten minutes and clarification of the supernatant liquid with Lloyd's reagent, maltose determinations were made on 5 c.c. samples of the clear filtrate by the Willstätter method.[11] This consists in adding 0.1 N. NaOH until the reaction is faintly blue to thymolphthalein, then exactly 3 c.c. in excess. Two c.c. of 0.1 N iodine solution are then added and the flasks placed in a water-bath at 20° C. for fifteen minutes. The mixture is then acidified with N. H_2SO_4 (1 c.c. for each 10 c.c. of NaOH used), and the excess iodine is titrated with 0.01 N. $Na_2S_2O_3$.

RESULTS AND DISCUSSION

Using the above procedure the following cereals were studied: Cream of Wheat, Mead's Cereal, whole wheat meal, corn meal, rolled oats, and quick oats. Four complete series of estimations were made on the first two cereals, and two series on each of the remaining four. The results are summarized in Table I and Charts 1 and 2.

From the table, and still more clearly from the charts, it can be seen that cooking five minutes in a double boiler brought about a very rapid increase in the ease of digestibility as shown by the amount of sugar formed under the stated conditions; that cooking for a total of fifteen minutes, and still further for thirty minutes, caused an appreciable but less marked increase; but that cooking longer than thirty minutes effected no significant increase in the amount of maltose

TABLE I

AVERAGE AMOUNT MALTOSE FORMED FROM ONE GRAM CEREAL AFTER VARIOUS PERIODS OF COOKING AND A UNIFORM DIGESTION PERIOD (THIRTY MINUTES)

TIME OF COOKING	CREAM OF WHEAT (MG.)	WHOLE WHEAT (MG.)	CORN MEAL (MG.)	MEAD'S CEREAL (MG.)	QUAKER ROLLED OATS (MG.)	QUICK QUAKER OATS (MG.)
Raw	4	5	13	11	25	29
5 min.	74	72	111	88	108	104
15 min.	106	105	126	115	117	133
30 min.	125	116	138	131	133	127
1 hr.	136	125	139	135	141	143
2 hr.	153	134	147	143	142	150
4 hr.	158	136	152	142	149	149

formed, except in the case of Cream of Wheat, in which there appears to be a slight increase up to the two-hour period.

In addition a precooked form of Mead's Cereal was also tested.* This product is prepared by cooking Mead's Cereal mixture in large

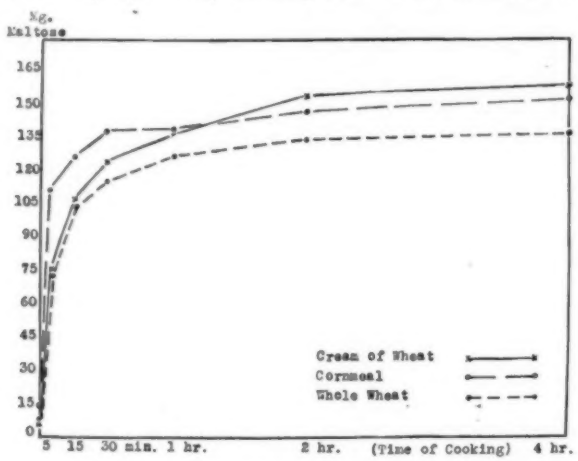

Chart 1.—Average amount of maltose formed from 1 gm. cereal (thirty-minute digestion period).

kettles under steam pressure for twenty minutes then drying on a drum dryer. Samples of this were weighed out and allowed to stand in 15 c.c. of cold water for one hour at room temperature. Without being subjected to any further cooking they were digested as in the case of the other cereals. Six estimations of the digestibility were made and the results are shown in Table II.

From Table II it is shown that when 1 gm. of the precooked cereal is digested thirty minutes 183.22 mg. maltose is produced. This is a considerably greater maltose production than is found when the same digestive procedure is carried out with any of the other cereals. It

*Pablum.

TABLE II

THE DIGESTIBILITY OF ONE GRAM OF PRECOOKED CEREAL MIXTURE AS SHOWN BY SUBTRACTION OF MALTOSE PRESENT IN UNDIGESTED CEREAL FROM MALTOSE FOUND AFTER THIRTY MINUTES' DIGESTION

	ZERO DIGESTION MALTOSE PRESENT (MG.)	30-MINUTE DIGESTION TOTAL MALTOSE FOUND (MG.)	DIFFERENCE MALTOSE FORMED (MG.)
	57.12	242.08	184.96
	59.84	247.52	187.68
	40.80	217.60	176.80
	44.0	225.0	181.0
	41.8	227.5	185.70
	41.8	225.0	183.20
AVERAGE	47.56	230.78	183.22

is possible that this increased digestibility of the precooked cereal is due to the method of pressure steam cooking to which it is subjected during manufacture.

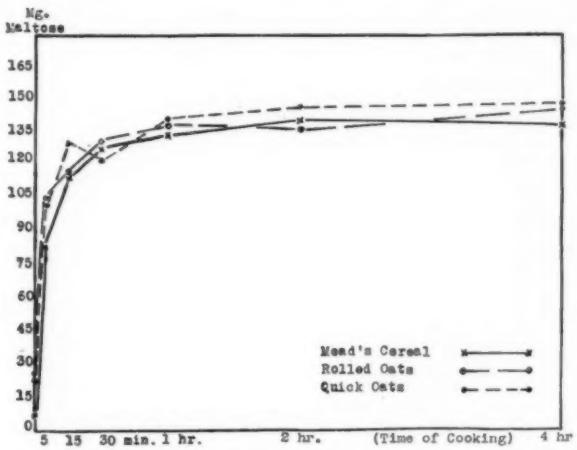

Chart 2.—Average amount of maltose formed from 1 gm. cereal (thirty-minute digestion period).

DETERMINATION OF TOTAL SOLUBLE CARBOHYDRATE FORMED BY DIGESTION

A report by Snyder[2] in 1902 stated that the digestibility of rolled oats was considerably greater following a four-hour cooking period than following a thirty-minute cooking period. He based this conclusion on his findings which indicated that there was over three times as much soluble carbohydrate formed by malt digestion after cooking four hours as there was after cooking for thirty minutes. It was thought advisable to repeat this type of experiment and determine the total soluble carbohydrate formed after varying cooking periods and a uniform digestion period.

Determinations of total soluble carbohydrate were made on two of the cereals, namely, rolled oats and Cream of Wheat. The method of preparing the cereals was the same as before, except that following digestion the digests were filtered through No. 40 Whatman filter papers, and the filtrate then hydrolyzed for three hours in a boiling water-bath with dilute hydrochloric acid which converts the soluble starch and dextrins to dextrose. The dextrose content of 2 c.c. portions of this solution was then determined and calculated as maltose.

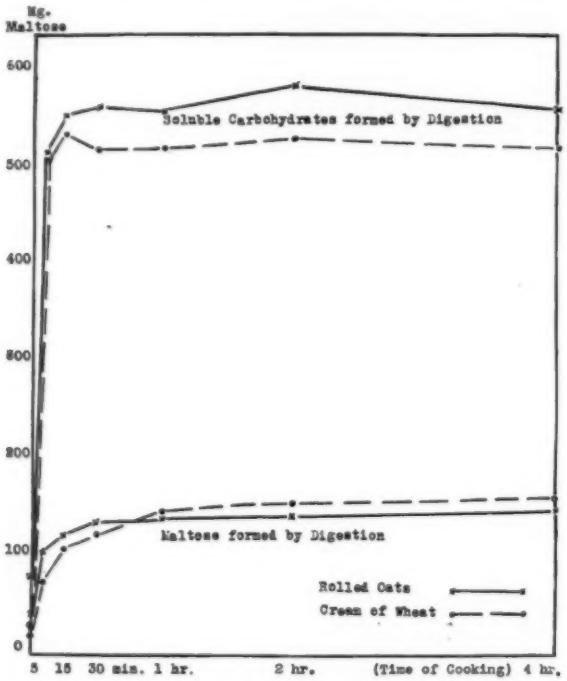

Chart 3.—The effect of various cooking periods on the digestibility of the carbohydrates of Rolled Oats and Cream of Wheat.

The results of these estimations are shown in Table III and Chart 3. It will be seen that there is considerable similarity between the curves of maltose production for a thirty-minute digestion period and the curves for total soluble carbohydrate formed after a similar digestion period, except that the magnitude of the latter is considerably greater (4.1 times).

We have been unable to confirm Snyder's findings that the digestibility of rolled oats was over three times as great after four hours' cooking as it was after thirty minutes' cooking.

TABLE III

TOTAL SOLUBLE CARBOHYDRATE FORMED AFTER VARIOUS PERIODS OF COOKING AND A UNIFORM DIGESTION PERIOD (30 MINUTES)

TIME OF COOKING	ROLLED OATS		CREAM OF WHEAT	
	TOTAL SOLUBLE CARBOHYDRATE (MG.)	AVERAGE (MG.)	TOTAL SOLUBLE CARBOHYDRATE (MG.)	AVERAGE (MG.)
Raw	81.6		44.0	
	76.2	73.9	21.8	32.9
5 min.	511.6		522.4	
	502.1	506.8	501.6	512.0
15 min.	557.0		597.2	
	536.6	546.8	470.4	533.8
30 min.	562.0		540.0	
	552.1	554.6	495.8	517.9
	549.8			
1 hr.	557.8		530.0	
	546.6	552.2	507.2	518.6
2 hr.	597.6		566.0	
	581.0	589.3	488.4	527.2
4 hr.	576.6		512.0	
	568.4	557.4	520.0	516.0
	527.3			

CONCLUSIONS

1. Cooking for more than thirty minutes in a double boiler did not significantly increase the digestibility of cereal starches as shown by the amount of maltose and of total soluble carbohydrate formed in vitro under standard digestion conditions.

2. No significant differences were found in the relative starch digestibility of Cream of Wheat, corn meal, Mead's Cereal, Quaker rolled oats and Quick Quaker oats. Whole wheat, however, was slightly less readily digested.

3. The starch digestibility of a special precooked cereal mixture was more rapid than the starch digestibility of any of the other cereals tested.

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THE DISCARD OF THE CRADLE

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THIS article will begin by paraphrasing a sentence from the work of the distinguished scientist, Prof. A. S. Eddington. The practice of pediatrics "would be stinted and narrow if we could feel no significance in the world" of childhood "beyond that which can be weighed and measured with the tests of the physicist or described by the metrical symbols of the mathematician."

In accordance with this thought I venture to drag a discarded piece of furniture from the attic and talk about it in the light of my experience as a pediatrician. This is not merely a sudden fancy of old age, it is a conviction of thirty-five years of observation.

However, before taking up the subject of the cradle, an introductory study on "amusing the baby" seems necessary.

AMUSING THE BABY

Probably some of our older pediatricians were not psychologists and may not have been versed in the folklore of amusements. Possibly they were influenced by such sayings as that of Pascal, "Amusement allures and deceives us, and leads us down imperceptibly in thoughtlessness to the grave." It seems they were not impressed by the admonition of Addison to "encourage innocent amusement." Or, were they so engrossed in the physiology and pathology of the body that the effect of psychic reactions to external stimuli was entirely ignored? It seems so. At any rate we find the following axiom laid down by a prominent pediatrician (Cotton) in 1900, "An infant during the first year should neither be amusing nor amused."

Such was the hard-hearted and inexorable maxim of a conscientious practitioner. Even at that time the grave consequences of institutional life were easily accessible, and the foundling or hospitalized infant served as an outstanding example of the neglected infant who had not been amused. Yet he inscribed this amazing precept in his book.

L. Emmett Holt as late as 1916 laid down this guiding rule, "Playing with young children, stimulation to laughter and exciting them by sights, sounds or movements until they shriek with apparent delight may be a source of amusement to fond parents and admiring spectators but is almost invariably an injury to the child."

Read before the St. Louis Pediatrics Society, December 4, 1933.

One looks in vain for clinical observations that support this emphatic proposition. When and where has the young child been harmed by shrieking with laughter? In fact, the most cursory observations among happy families would throw serious doubt on this unqualified statement.

Recent textbooks give more space to the value of play in developing the child, and yet the warning against amusements is not wholly eradicated. Thus Griffith and Mitchell* in the textbook of 1933 state: "Amusements begin early, and those may be gradually added which educate the mind to a certain extent. Yet the training of the mind must always hold a secondary place, lest overstimulation of it result. In fact, all amusements which cause much excitement are to be avoided, and this is especially true just before bedtime, or insomnia will naturally result."

Thus considerable stress is still laid down on the harmful effect of a "good time" just before bedtime. The young father at home from his daily vocation wants to play with the baby, but play at that time is interdicted by the modern trained mother. Hence, so many fathers never have a chance to become acquainted with their children.

The young child likes to play after supper, and as a rule, by bringing on a sense of fatigue, the sport promotes rather than inhibits healthy sleep. Of course, this can be overdone, but my observation leads me to believe that this rarely happens except on festival occasions, as the night before Christmas.

Now compare the quotations from pediatricians with the statements of Katherine Oettinger (Hygeia, December, 1933), "Play is just as important a part of baby's life as sleeping or eating. Baby must feel happiness after he has done the thing you are teaching him."

We pediatricians have really done harm by the excessive emphasis laid on the possibility of "spoiling" the child. How often have we seen an infant, four or five months old, laid in the crib with his bottle and no attention paid to him, or placed in another room at bedtime and the door closed! This is not care; it is absolute neglect of the infant. Fortunately, the parent's love in most cases has not acquiesced in these iron-bound rules. The fond mother keeps an eye on her infant, and the grandmother cannot endure its cry. We have been too hard on grandmothers! It is a perfectly natural impulse of maternal love to please the baby. What right have we to overrule this natural impulse?

I have felt a great deal of satisfaction from the recent publication by Dr. Knight Dunlap, Professor of Experimental Psychology at Johns Hopkins University (Science News Letter, June 10, 1933). He criticises certain regulations recommended by some influential physicians and pronounces some of these so-called scientific methods as systematic neglect, to quote him: "The baby which is neglected does in the course of time adjust itself to its unfortunate environment. Such babies become good babies and progressively easier to neglect. Such procedure is no more

*J. P. C. Griffith and A. G. Mitchell: The Diseases of Infants and Children, 1933.

justified by these results than is the method of keeping the baby mildly drugged. The baby should not be allowed to cry, or rather crying should be minimized, and never allowed to continue long."

Another common dictum found in nurses' textbooks on nursing is that the baby should amuse himself, and for this purpose some toys are placed in the crib. Is this not another form of willful or unavoidable neglect? Dr. Dunlap gives a clear statement on this practice: "The baby should be allowed to amuse itself only for short and carefully controlled periods. It should be amused during practically all of its waking time."

I believe every pediatrician who has children of his own and has watched the growth of children in the homes of the middle class will concede this point. How can the baby amuse itself unless some one teaches and demonstrates the steps of the play? Even the adult finds any sort of sport or play dull and tiresome when alone. And should we expect more from the baby?

But the great objection is that you will spoil the baby by paying too much attention to it. Perhaps, this is sometimes true. Here is what Dr. Dunlap writes: "Of course, keeping the baby happily stimulated during its waking periods and preventing crying, while not 'spoiling' the child is a difficult task; too difficult, perhaps, for the intelligence of the parents. Spoiling the child, however, is a minor evil, neglecting it is a major one."

I am inclined to believe that this great fear of overstimulation should be placed in the same category as overfeeding which was expounded with such emphasis only a decade ago. Of course, there is danger of overfeeding but it is insignificant compared with the destructive effect of underfeeding. There may be some danger in overstimulation, but its ultimate consequences are trivial compared to the backwardness produced by continuous understimulation.

When should this playing with the baby begin? My answer is as soon as the baby responds in a happy way to external stimuli. The first play is to be carried around to different lights, different movements, and different scenes. Soon come toys, and the baby is shown how to use them. While the play is primarily prescribed to encourage exercise and teach useful movements of the body, a psychic stimulation invariably goes with this. It is desirable that the exercises produce joy and not distress. Instinctively the parents want the baby to smile and later laugh heartily. Every infant should be enticed to smile or laugh every day. We have often encountered neglected infants who rarely or never laugh or smile. I have seen these same infants develop into children who lack the exuberant hilarious spirit of the normal child.

I venture, therefore, to propose a new precept by contradicting the axiom of Dr. Cotton: "An infant during the first year of life *should* be amusing and be amused."

As a matter of practice, I believe, we can safely leave the question of amusement of children to the parents. The infant practically always responds to overstimulation by a cry of anger or distress, and then the stimulation stops abruptly. Most parents soon learn when the baby gets tired of the game. Why should the pediatrician circumscribe this activity with gratuitous regulations based on prejudicial or, at least, on shadowy hypotheses!

THE CRADLE

What a folklore has accumulated about the cradle! Most of us remember only Wallace's famous distich:

> "For the hand that rocks the cradle
> Is the hand that rules the world."

Perhaps we have not forgotten that beautiful poem of Elizabeth Allen:

> "Backward, turn backward, O Time, in your flight
> Make me a child again just for tonight."

Each stanza ends in that soothing refrain:

> "Rock me to sleep, mother, rock me to sleep."

We still laugh over the speech of Mark Twain given in honor of General Grant in response to the toast, "The Babies." He mentions the "three or four million cradles now rocking in the land." This was in 1879. Ten years later the general destruction of the cradle began. This was accomplished at first only in foundling homes but also spread to the baby hospitals and obstetric departments of the hospitals. It seemed so unnecessary to rock the newborn. By 1890 the trained nurses from such institutions were beginning to attack the use of the cradle even in the home. They had become firmly imbued with the idea that the baby's principal complaints were due to overindulgence by fond parents. The cradle was the first step in spoiling the baby, and hence this practice must be destroyed at its incipiency. For example, Lisbeth D. Price in her textbook of nursing (1892) specially emphasizes in italics that the baby "should never be rocked nor hushed on the nurse's neck."

I had the opportunity to follow this attack on the cradle during my early professional career. It seemed to me then that the greatest influence emanated from the babies' hospitals in New York, Philadelphia, and Chicago, since many of the writers in our prominent women's magazines had received their training there. In the nineties all these magazines published numerous articles on the care of the baby. Many of these contained vicious attacks on the use of the cradle.

The greatest influence, however, was exercised by the textbook of Dr. L. Emmett Holt. In the first edition (1897) we find this statement: "To induce sleep, rocking and all other habits of this sort are useless and may be harmful. I have known of one instance where the habit of rocking

during sleep was continued until the child was two years old; the moment rocking was stopped the infant would awake."

At another time he wrote (1916), "The crib should be one that does not rock in order that this unnecessary and vicious practice may not be carried on."

Holt's teachings were widely circulated through his mother's guide, "The Care and Feeding of Children" (1910). In this he answers the question, "Is rocking necessary?" "By no means. It is a habit easily acquired but hard to break and a very useless and sometimes injurious one."

If we study subsequent textbooks by various writers we find a similar warning. Lucas makes it very emphatic. "The hand that rocked the cradle has happily passed out of the modern nursery. No baby should be rocked, petted or otherwise entertained while he is going to sleep." Chapin and Royster are much milder in their directions, "Rocking as a preliminary or accompaniment of sleep is undesirable." The tenth edition of Holt has practically the same instruction on this practice as the first. The new textbook of Griffith and Mitchell has this statement: "Walking the floor, rocking, singing to sleep, and the like are entirely unnecessary. They establish the child in a bad habit and make a slave of the mother."

Ramsay, in Abt's Pediatrics (1923), expresses the usual thought, "The old habit of rocking or walking the baby to sleep is a pernicious one and has nothing to recommend it."

Finally I quote from the standard nursing textbook on pediatrics by Bessie Cutler (1927), "The child must never be rocked to sleep, given a pacifier or any soothing device."

It seems to me that many of these statements are but echoes of the past. There was a time when nurses felt that the infant life could be regulated by scientific rules even in every home. Did we not prescribe a definite quantity of food made up of an accurate composition? Have we not tried to regulate the hours of sleep and exercise? Did we not repress the desires of the growing infant into a narrow groove? Did any trained nurse or pediatrician ever inquire of the mothers of two or three children whether or not she found the cradle helpful in the care of the baby?

Many years ago I wrote an article on the cradle protesting against the general expulsion of this convenient and inexpensive furniture from the nursery. The older child has his rocking horse, swing, kiddy-car, or scooter; the baby has a rigid iron bed, the crib, or the bassinet.

I desire once more to bring up the subject of rocking in infancy, and give some clinical impressions why this subject should not be dismissed as fully settled. I will concede at the outset that rocking is usually unnecessary. Necessity is, however, not the only reason for establishing certain practices. Every one can easily recall many diversions of our

childhood which were very pleasant but really not necessary. Probably most of the toys given to children are not necessary. Playing or amusing the baby are really not necessary. The baby learns to adjust himself to all kinds of parental neglect, as Dr. Dunlap so tersely stated.

We can dismiss the alleged injurious effect of rocking with a few sentences. The only bad effect observed by any one is that the practice may become a habit which is hard to break. But is not this also true of breast feeding, bottle feeding, and other practices in infancy?

Another objection is that this spoils the baby. It is contended that the healthy baby should fall asleep without any soothing measures. But does it? It is generally acknowledged that the deep sleep of childhood does not manifest itself until later. As a rule babies are poor sleepers. True, the baby may become exhausted from crying itself to sleep, but few parents have the hardihood to endure this without making some effort to soothe the baby. I feel that Dunlap is correct in teaching that crying in a baby should be minimized. Soothing some babies to sleep is good practice.

Here I wish to lay stress on the favorable effect of rocking on the life of the young infant. I must admit that the conclusions are based entirely on clinical impressions. But was it not the clinical impression of some nurses and physicians which abolished the use of the cradle?

Let us recall briefly the more obvious physiologic effects of rocking. It has a cooling effect since the motion acts as a gentle fan and hastens evaporation from the skin. The gentle swaying motion has a soporific influence. It is distinctly soothing to the excited nervous system.

There is, however, one effect which, it seems to me, has been entirely overlooked; namely, the assistance to the pendular movements of the intestine. In addition to the chyle the intestine always contains gas, and the swinging movements of its body causes the liquid chyle to gravitate backward and forward over the intestinal mucosa. Rocking, therefore, is a physical therapy which aids digestion and probably absorption. It is precisely the young infant who suffers from intestinal dyspepsia especially when breast fed.

The many jokes on the young father and the dyspeptic baby have their source in actual experience. The spitting up, the violent attacks of colic, the insomnia, the distended abdomen, the passage of flatus, and the mucoid thin stools are the principal diagnostic symptoms. It would lead too far in this paper to offer an explanation of these symptoms. As a matter of fact, the actual mechanism is not really understood and gratuitous hypotheses are numerous. But I have certainly obtained the clinical impression that young infants who are rocked after nursing as a rule have less colic, less enterospasm and become happier babies than those who are laid in the crib without rocking. In fact, I have several times availed myself of this physical therapy even in recent years to re-

lieve the dyspeptic young baby. But it is difficult to procure a cradle now. Again and again I could not prescribe rocking because a cradle could not be found.

Stress must be laid, then, not on rocking the baby to produce sleep, but rocking the baby to relieve certain annoying digestive symptoms. The baby is rocked not necessarily at its sleeping time but after a feeding. When the symptoms are relieved, the baby goes to sleep.

In my opinion the total discard of the cradle has at least aided in two unfortunate results; first, there has been a definite increase in bottle-fed babies, and second, an increase in umbilical hernias.

The insufficiency of the mammary function in our modern young mothers is too serious even to allow words of derision or merriment. By far the most common cause is, to use the language of the laity, the fact that the milk does not agree with the baby. The dyspeptic symptoms are so violent, the baby cries day and night and, consequently, the baby is put on the bottle. Many of these unfortunate results can be prevented by rocking the baby after nursing. I firmly believe that the cradle assists maternal nursing.

The second effect, the more frequent occurrence of umbilical hernias in the modern infants, has a partial explanation in the increased flatulency in the unrocked babies. Rocking, by increasing peristalsis and food absorption diminishes the formation of gas, and the increased pendular movement facilitates its expulsion.

In actual experience rocking has not been abolished. We find the majority of mothers wheeling the crib back and forth, jolting the mattress up and down, or swinging the baby in a rocking chair. The baby carriage has become a common bed for the baby and jolting the infant up and down on the springs is a very common practice. None of these, however, can take the place entirely of the easy side-to-side movements of the cradle. The common use of the pacifier and the frequency of thumb-sucking also reveal that well-known soothing measures are still employed.

The question of the cradle, that is the physiologic effect of rocking, is really a good subject for scientific research. If these remarks will stimulate some worker to undertake such a study, the purpose of these remarks will be accomplished.

Here some quotations from two old masters, who were backward in science but proficient in domiciliary practice, may be interesting:

"There has been at all times a considerable expenditure of words, and much learned trifling with regard to the question of the salubrity or insalubrity of cradles. It appears to us that their employment or nonemployment is a matter that may very safely be left to the fancy or convenience of the parents. A cradle makes a clean, airy, and, from the facility of moving it about, a convenient bed. As to the injury likely to

be inflicted upon the central nervous system by rocking, we have not the shadow of a proof that such species of motion is ever injurious to the brain." (Evanston and Mannsell, 1842.)

"A cradle for young children is a very important appendage to the nursery, notwithstanding the objections which have been made against it, by ingenious speculators upon the subject of the physical education of children. The advantages of the cradle are: first, it can be placed in any situation in the room without disturbing the child, for the advantage of either warmth or coolness, for light or darkness, or for air; second, it supplies the most gentle and certain anodyne, if we may so term it; since it will amuse by its motion when the child is placed in it awake, lull by its sameness when disposed to sleep. The objections to the use of the cradle are easily obviated." (Dewees, 1847.)

Apparently, the same professional attitude which originated the celebrated maxim of Cotton also was responsible for the destruction of the cradle. Some day, I believe, it will be no disgrace to rear the young baby in a cradle and even sing him to sleep by a lullaby.

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CHICKENPOX IN AN EIGHT-DAY-OLD INFANT

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ON JANUARY 2, 1934, I was called to see a four-day-old infant in the Out-Patient Obstetrical Service of the Presbyterian Hospital, Chicago. The child at that time showed no abnormalities whatever except a slight phimosis. He weighed 8 pounds; stools were normal and he was nursing well at the breast. There were no lesions of any sort on the skin.

Eight days later, the same infant, then thirteen days old, presented a very different picture. The entire surface of the body presented an eruption characteristic of varicella at the height of its eruptive stage. The lesions were of the macular, papular, pustular, vesicular, and crusted variety. Vesicles and crusts were especially prominent on the trunk and scalp. The lesions seemed to lie on the skin and not deep in the tissue. The crusting, though definite, was apparently not of long duration. None of the scabs could at this time be brushed off. The larger vesicles were about 1½ cm. in diameter. Occasional umbilication was observed. The vesicles contained a thin, yellow, serous fluid and were in places confluent; chiefly on the anterior chest and scalp. Pustules, though present, were quite infrequent. The palms of the hands and soles of the feet were affected. Flat red spots intermingled the older lesions over the entire body. The external ears and nares were partially occluded by the presence of thin-walled vesicles and semi-solid, newly formed crusts. Several cutaneous ecchymotic and bleeding areas were noted on the face, particularly at the palpebral margins. The lips were dry and chafed without discrete lesions. The oral mucous membranes were also involved. The tongue was rather dry and papilla prominent. Maculopapular, roughly circular white patches of various sizes could be seen on the buccal mucosa. They were most plentiful in the palatine region. The posterior pharynx was injected and patchy. The general odor was slight. Rectal temperature was 98.6° F.; heart rate was 174; lungs were clear. The infant was alert and not inactive, became irritable when disturbed and was assumedly very uncomfortable. Earlier in the day the patient had nursed at the breast eagerly and taken water freely. Only for the two previous days had he been reluctant to take his feedings. The general constitutional signs of an acutely ill infant were lacking.

The day before this examination (January 1, 1934), a private physician had been called to see the newborn infant. A diagnosis of impetigo contagiosa had been made and calamine lotion prescribed. The lotion had been sparingly applied. The infant seemed relieved.

The most likely diseases to be considered in this instance were variola, varicella, and impetigo contagiosa. The history was of importance in making a differential diagnosis.

They were a family of four, including mother, father, newborn infant, and a two-year-old son. The father was the only member of the family that had once had chickenpox and had been vaccinated for smallpox.

On the eve of December 28, 1933, the mother, a white American multipara, twenty-two years old, delivered the infant. Delivery in the home was normal and not remarkable. A slight rise in temperature was recorded by the visiting nurse for the four days following delivery, the highest being 99.4° F. on the second postpartum

day. Pulse and respirations did not fluctuate from normal. On the fifth postpartum day the temperature was 98° F., pulse 84, and respiration 20. The mother at the time of delivery recalled mentioning to the district physician in charge that she had noticed "several red spots" on her left thigh. She neglected, however, to mention the fact that on December 8, twenty days before her confinement, a neighbor child living under the same roof had been ill for a few days with fever and eruption. (This case was also diagnosed impetigo by the private physician.) Further, the mother did not mention that on December 18, ten days after the neighbor's illness and nine days before her confinement, her two-year-old son had a similar episode with fever and eruption. The son was not confined to bed. His temperature was not taken. He was, "under the weather" for only a few days and "broke out," as did the neighbor child. A doctor was not called. The lesions disappeared by forming crusts and dropping off. They left three or four shallow-pitted scars in each case.

The red spots on the mother's thigh proved to be the first crop of a chickenpox eruption. On the fourth postpartum day the reaction was at its peak with macules, papules, and vesicles. They later dried, formed crusts, and dropped off. Itching was her only complaint.

The infant suckled and thrived until the morning of the eighth postpartum day (January 6) at which time the mother first noticed red spots on his body. These progressed in the same manner as the others to present the picture previously described. The infant made a rapid and uncomplicated recovery.

We have here, a fairly clear-cut progression of events with four individuals involved. The history, the very mild symptoms, the appearance of successive crops of superficial vesicles, the formation of crusts, and the rapid recovery in all four cases warrant the diagnosis of chickenpox.

Lesions on this newborn infant were first observed on the eighth day after birth. In all probability, the infection was transmitted from the mother to the child in utero—congenital chickenpox.

The incubation period of varicella is somewhat variable. Gregory[11] says it does not exceed four days and is certainly less than seven. Modern writers do not agree with Gregory.

Their beliefs are as follows: Trosseau,[11] twelve to twenty-seven days; Osler,[13] ten to fifteen days; Holt,[12] fourteen to sixteen days; Mitchell,[5] fourteen days; Jeans,[4] fourteen days; Grulee,[1] fourteen to sixteen days; Gee,[10] "At about a fortnight"; Thomas,[6] thirteen to seventeen days; Delpech,[6] twelve days; Corlett,[6] ten to nineteen days; Schamberg,[6] fourteen to seventeen days; Woody,[9] eleven to twenty-two days; Dock,[8] ten to twenty-one days.

Quoting from Sherman:[7] "The older authorities declared that the period of incubation lasted from four to six days. Steiner by inoculation, demonstrated it to be eight days. More recently, with the infection traveling in ordinary ways, it has been considered to vary from eleven to twenty-five days, but is oftenest fourteen to sixteen days."

Schamberg[6] says the earliest age at which varicella has been observed and recorded is the one reported by Senator, who saw an infant of eleven days with the disease.

S. S. Woody[9] believes chickenpox occurs rarely before the sixth month of life, although instances are recorded of newborn infants developing the disease as early as the eleventh or fourteenth day, having been infected from the mother.

Lereboullet and Moricand[3] have reported a case in an infant whose mother had chickenpox before the child was born. The infant did not develop the infection until the fourteenth day after birth. Grulee[1] believes that this case was one in which the child was infected by the mother, but that the infection was *not,* in all probability, transmitted in utero.

Pridham,[2] in 1913, reported the first case of congenital chickenpox. His patient was born with the typical eruption of varicella present, the mother having had the disease fourteen days before her confinement.

This case is reported because it illustrates a common error in diagnosis. It brings up the question of incubation and inoculation periods which modern authorities believe to be about fourteen and eight days, respectively. It is seemingly the earliest instance on record of the occurrence of chickenpox in a normal newborn infant. (Pridham's[2] case being one in which the eruption was present at birth; Senator's[6] patient developed the disease on the eleventh day.)

Lastly, it is confirmatory evidence, if not proof, that congenital chickenpox may occur.

We wish to express our appreciation of the time and advice given us by Mr. Asa Bacon and Mr. Herman Hensel, Superintendent and Assistant Superintendent of the Presbyterian Hospital, Chicago.

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Pediatric Clinics

THE PEDIATRIC CLINIC OF THE YALE UNIVERSITY SCHOOL OF MEDICINE

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THE Pediatric Clinic of the Yale University School of Medicine comprises the Department of Pediatrics of the University and the Pediatric Service of the New Haven Hospital and Dispensary. The Clinic has special liaison with the Department of Psychiatry and Mental Hygiene and the Clinic of Child Development of the University, and with the Children's Community Center of New Haven (a child-placing agency with extensive foster home and institutional facilities for convalescent children) and with the U. S. Children's Bureau.

HISTORICAL

The Medical Institution of Yale College, the parent organization of the present school, was formally opened in 1813 and in order of seniority is the fourth extant medical school in the United States. Teaching in pediatrics was inaugurated early, possibly from the very beginning, with lectures by Eli Ives, M.D., "Adjunct Professor of Materia Medica and Botany" in the original faculty. In 1820 Ives became "Professor of Materia Medica and Botany and Lecturer on Diseases of Children"; but he had taught the subject prior to this time, for there are extant, under date of 1816, notes by a student on Ives' lectures on diseases of children. Later, teaching in diseases of children was added to the duties of the incumbent of the professorship of "Obstetrics," which in 1868 became "Obstetrics and Diseases of Women and Children."

However, it was not until 1886, the year that the Medical Institution of Yale College became the Yale Medical School, that under "Course of Instruction" there was inserted in the school announcement a special notation concerning children. It appeared in the outline of the teaching in "Obstetrics and Diseases of Women and Children" and was as follows:

"*Diseases of Children.* This important branch of medicine is taught by didactic lectures and recitations, as well as by clinical instruction at the Dispensary and Hospital."†

In the bulletin of the Medical School for 1898-99 there appeared the following announcement under "Course of Instruction for the Senior Year."

"*Pediatrics. Recitations,* 1 hour first term, Professor De Forest.

Clinic, 1 hour throughout the year, with *section work,* second term, Dr. Bishop."

Dr. De Forest was "Clinical Profesor of Medicine" and Dr. Bishop was "Assistant in Pediatrics." This paragraph is noteworthy for the appearance of the title, "Pediatrics," and the indication that the work with children had been transferred from the chair of "Obstetrics and the Diseases of Women and Children" to that of the "Theory and Practice of Medicine."

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†Jacob introduced bedside teaching in Diseases of Children in New York in 1860.

Teaching and service in pediatrics remained a part of the functions of the Department of Medicine until 1921 when a separate Department of Pediatrics was created in the School of Medicine and a distinct Pediatric Service was organized in the New Haven Hospital, both under Professor Edwards A. Park.* Appointments to the hospital staff are made on nomination by the University.

The Hospital Service has the medical care of all patients under thirteen years of age, including newborn infants and children suffering from contagious diseases. Children on the Surgical Service are seen only on request. The Department of Pediatrics is one of five independent major clinical divisions of the Medical School and Hospital; these divisions taken as a group constitute the "Department of Clinical Medicine of the Graduate School of the University."

PHYSICAL FACILITIES

The New Haven Hospital was founded in 1826, but the present plant dates from 1930. The accompanying figure shows the plan of a portion of the third floor of the

The New Haven Hospital

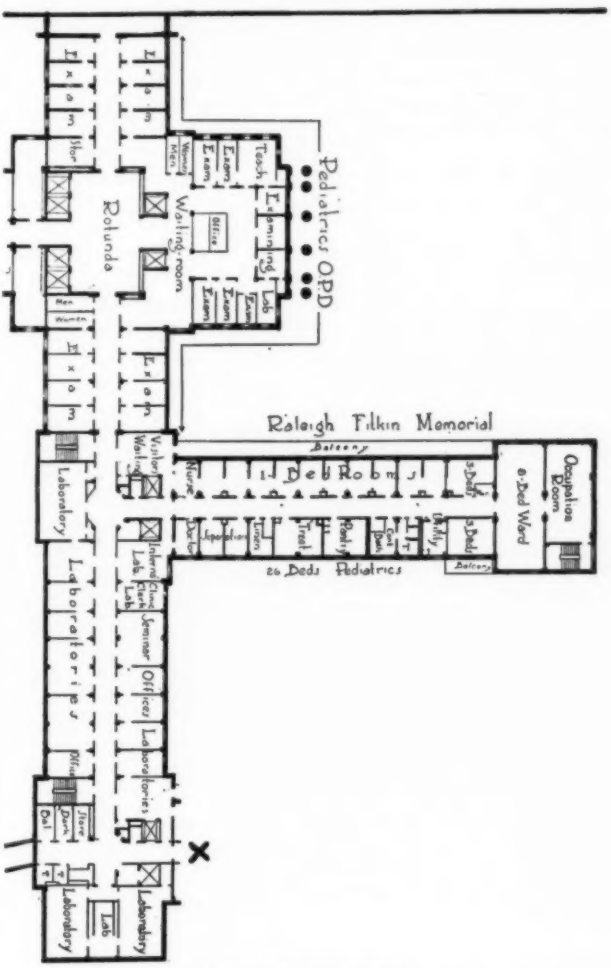
Hospital. The third floor of the central building of the medical-pediatric pavilion (The Raleigh Fitkin Memorial Building) and of the Laboratory for Medicine and Pediatrics are assigned to Pediatrics; also, the fourth floors of the Fitkin and Laboratory buildings. These facilities thus constitute a compact, two floor unit. Plans for the ultimate development of the Pediatric Clinic call for the use of both of the present wards for noncontagious cases and the construction of two similar wards for contagious cases at the point marked "X" on the floor plan. The wards and laboratories will then constitute the third and fourth floors of an open quadrangle, with the Out-Patient Division in physical continuity on the third floor of the adjoining building.

The nursery for newborn infants is in the maternity ward which is on the fourth floor of the surgical-obstetric pavilion; this pavilion is on the southeast side of the

*Dr. Park resigned in 1927 to accept the professorship of pediatrics in the Johns Hopkins University.

main, central building in a position corresponding to that occupied by the medical-pediatric unit. Six hundred and fifty infants were born on the Obstetric Service in 1933.

The Milk Preparation Laboratory is on the sixth floor of the central building in horizontal contiguity with the dietetic laboratories and the main kitchen of the



The New Haven Hospital

Floor plan of portion of third floor, allocation to Department of Pediatrics (similar allocation on fourth floor excepting Out-Patient Department)

Hospital, and directly above the pediatric wards. The preparation of milk mixtures is under the supervision of a special dietitian, who gives instruction to clinical clerks on the preparation and costs of special foods for infants.

The Out-Patient Division is physically and medically integrated with the other aspects of the work of the Clinic. The division has a full-time medical director;

the social service worker and Supervisor of Nurses for Pediatrics are the same for wards and dispensary. Each interne while on ward service sees his own discharged patients when they return to the Dispensary; a measure of medical continuity for such patients is thus attained. Each child with his parents or guardian is assigned his own examining room. By this arrangement privacy, self-respect, control of contagion, more adequate, intimate teaching are fostered and facilitated. Clinical laboratories for physicians and clinical clerks, and special rooms for treatment and for group demonstrations are available. The physician-in-charge, the head nurse and the social worker have private offices. A large waiting room is not needed because patients come by appointments, which are arranged in staggered order. Morning hours are given over to general cases and afternoon periods to special clinics. There were 12,000 visits to the Pediatric Out-Patient Service in 1933.

At the entrance to the wards, in connection with the head nurse's office, are waiting rooms for parents and other visitors. Across the corridor is the doctor's office contiguous with his clinical laboratory and that of the clinical clerks.

The balconies with southern exposure are easily accessible for all patients through triple-sashed windows. The rooms marked "separation" are air-conditioned for the care of premature and feeble infants. The single rooms are available for infants and for very sick older children. The larger units afford opportunity for companionship among the patients. Running water is available in all units, and the first four single rooms are equipped with toilets so that they may be used as "observation" rooms for newly admitted patients.

The usual capacity of the wards is from twenty-five to thirty patients. The number of beds assigned to infants and to children is not fixed but fluctuates according to demand. In 1933 there were 335 admissions on the infectious disease service and 239 on the noninfectious service.

Private patients are cared for in a special pavilion built for such patients, children and adults alike.

The room marked "seminar" is The Pediatric Study, a simply but attractively furnished library and sitting room, which is the physical center of the Clinic. The equipment was the gift of women physicians connected with the Department, 1921-30. The study contains the department library of reference books and current journals.

The room marked "laboratory" at the end of the ward is a large teaching room where student and staff conferences are held. A large amphitheatre is located on the first floor of the Medical and Pediatric Laboratory.

The laboratories for research and routine studies on the third floor are equipped for chemical investigations while those on the fourth floor are designed for bacteriologic work. On the roof at the end of this floor is a penthouse which contains animal rooms with outside runways.

Studies involving roentgenographic, electrocardiographic, and postmortem examinations are carried out in collaboration with the departments in which these technics have been developed. In 1933 there were autopsies on twenty-four newborn infants and on fifty-two other children.

STAFF

At the present time the Staff consists of thirty physicians. Six of these are salaried and devote their time to work in the University and Hospital; fourteen give part-time service to the Clinic on a voluntary basis; ten are members of the house staff, whose appointments are for one year.

Technical assistance is provided in both the chemical and bacteriologic laboratories.

Of the salaried physicians, one has charge of the bacteriologic laboratory in the department and another of the chemical laboratory. These, with some of the others

in this group (including a Fellow) are engaged primarily in investigative work, with limited administrative and clinical responsibilities.

The policy of having department laboratories of bacteriology and chemistry instead of a central hospital laboratory is worthy of comment. The men who head these departments have direct clinical interest and responsibility for the patients on whom bacteriologic and chemical studies are done. As a result there is close correlation of clinical findings, laboratory data and therapeutic procedures. Scientific inquiry is stimulated in this way, and the members of the house staff are encouraged to become acquainted with routine laboratory procedures and with the interpretation and significance of more elaborate studies. By way of illustration: it is felt that the house staff should be able to do certain chemical procedures such as blood sugar determinations and should know the technic of planting and examining bacteriologic cultures such as are taken from throats, spinal fluids, and blood. Laboratory assistants, as well as physicians, are available for guidance of junior men.

There are six internes on the house staff; they rotate in their experience and responsibility. The allocation of time is as follows: infectious disease ward, four months (two physicians); noninfectious disease ward, four months (two physicians); out-patient service (including work in the Nose and Throat Clinic) and nursery for newborn infants, two months (one physician); and Children's Community Center, two months (one physician). When on the latter service the interne has charge (under a resident who is also a member of the department staff) of cottages for convalescent and crippled children and makes house visits to children in foster homes. Also, on this service, routine health examinations are made, and various preventive procedures performed.

Preferably, internes are chosen from men and women who have just graduated from medical school, but no fixed rule is followed.

The senior assistant resident has a year's service as assistant to the physician-in-charge of the Pediatric Out-Patient Service. The two junior assistant residents alternate in charge of the infectious and noninfectious service.

The resident has general medical supervision of ward patients and administrative and teaching responsibilities.

Time and opportunity are available for investigative work by members of the house staff, particularly the assistant residents, who are interested and qualified.

The physicians who give their services on a voluntary basis make contributions of inestimable value to the Clinic. In addition to dispensary work and to ward and office teaching of students of the graduating class, these physicians bring special contributions to the department, notably the point of view and procedure of the private practitioner. One clinical professor is medical director of the infant welfare conferences of the local visiting nurse association, and another clinical professor has a similar relationship to the Children's Community Center. These relationships give the Clinic close affiliation with highly important health organizations. Other members of this group have important positions on other health and social welfare activities of New Haven and Connecticut.

A noteworthy feature of the department is the cooperation with the Department of Psychiatry. A psychiatrist specially trained in both pediatrics and psychiatry assists in the understanding and treatment of children with behavior problems. This physician attends pediatric conferences and teaches students in certain of the courses in the Department of Pediatrics. A similar liaison exists with the Clinic of Child Development. Developmental studies as indicated are made on patients on the Pediatric Service, and assistance is rendered in interpreting certain psychologic and developmental phenomena. The Nursery School of the Clinic of Child Development is available for observation and treatment of certain children.

The department has cooperated actively with the Children's Bureau of the U. S. Department of Labor in neonatal and rickets studies. Professional members of this staff have offices in the department; they share in clinical work and in teaching, paying special attention to the aspects of pediatrics in which they are making studies. These responsibilities are of value to investigator, Clinic and student alike.

NURSING

The Nursing Service of the Clinic in all divisions is under the Supervisor of Pediatric Nursing so that coordination and integration of all pertinent nursing activities are fostered. The Pediatric Wards are sufficiently staffed, so that it is possible both to give adequate nursing care to sick infants and children and to carry out the principles of child management and habit training, which are advocated by the Nursery School and Clinic of Child Development. The appointments for patients in the Dispensary are under the Nursing Service. The supervisor is an instructor in the School of Nursing and teaches medical clerks in certain aspects of child care and treatment. Similarly, instructors in the Department of Pediatrics share in the teaching of students in the School of Nursing. The instruction of parents in child care is a cooperative function of the Nursing and Pediatric Services.

SOCIAL SERVICE

The Pediatric Service has the cooperation of medical-social service as an integral part of its work. Cases for social study and treatment are referred by the physician to the medical-social worker, and thereafter frequent conferences between the social worker and the physician are held in order to correlate the medical and social care of the patient. The social worker makes regular rounds with the house staff and attends conferences on discharged patients. Social summaries are placed by the social worker in the unit medical histories giving what social data might be helpful to the physician. Students have contact with social workers in the Dispensary and in special conferences described later.

Under Medical-Social Service and the Nursing Service are volunteers who carry out special follow-up work on cardiac cases or recreational work for children, either on the ward or in the clinic. This latter work is done by a group of interested women comprising the Children's Recreational Committee; through its activities, occupational therapy, recreation, and good cheer are brought regularly to many sick children. Birthdays and other holidays are especially recognized.

The New Haven Department of Education details to the clinic a special teacher who gives instruction to appropriate cases during the year.

UNDERGRADUATE INSTRUCTION

During their first clinical year students serve ward-clerkships (morning session) for five weeks in pediatrics. Daily ward conferences during that period in which the senior staff participates are not primarily concerned with bringing pediatric problems to the fore but rather, by "joining in" with instructors from other departments, in focusing attention on fundamental principles of clinical medicine. Attempt is made, however, in cooperation with the Supervisor of Pediatric Nursing, to teach the technics of infant and child care and some of the more common procedures used in treatments of various types.

In the second clinical year, the year of graduation, emphasis is placed on problems peculiar to the developing child. Students serve clerkships (morning session) for five weeks in the Dispensary. During this period they also attend daily conferences on ward patients. For the most part these conferences are conducted by attending physicians who practice pediatrics in the community. These physicians take the group of students for a week (one hour daily); sometimes the students are taken to the office of the practitioner. All of these physicians do not participate in

the teaching of any one group of students, but each group has a week of conferences with the physician interested in diseases of the newborn and a week with the instructor from the Department of Psychiatry, who is specially interested in the behavior problems of children.

One hour each week also is given to a conference with the Director of the Social Service Department of the Hospital and the social worker attached to the Pediatric Service in conjunction with the physician-in-charge of the Pediatric Dispensary. The students and the social worker present selected cases for discussion primarily from the angle of social adjustment.

There is a weekly clinic at which various pediatric problems are discussed and illustrative cases presented; these clinics are attended by students in both clinical years.

The work just outlined constitutes that usually designated "required"; in addition, elective courses in pediatrics are offered, most of which are open only to students of the second clinical year. There is a seminar course in physical and mental development of infants, their metabolism, nutrition, and feeding and in diseases of the newborn. The course is one hour per week throughout the academic year; the discussions on mental development are given by the Director of the Clinic of Child Development. There are two shorter seminar courses, one in clinical bacteriology and the other in infectious diseases. There are elective dispensary courses in infant welfare, in tuberculosis, allergic conditions, syphilis, diseases of the newborn, of metabolism, and of the heart.

Before graduation students are required to present a thesis; the work described in the thesis is done in one or another of the departments of the Medical School. The Department of Pediatrics shares, of course, in giving direction and leadership in this work to a certain number of students. Much of the work is published.

GRADUATE INSTRUCTION

The policy of the department in respect to graduate instruction is that the most satisfactory means of acquiring facility in the practice of pediatrics is through the discipline of interneships and residencies on a Pediatric Service. The department, however, fosters contact with practicing pediatricians, who are invited to the weekly clinics. At special "rounds" once a week and at the weekly conference on discharged cases, visiting physicians are specially welcomed; many physicians from the city and from various parts of the state attend these exercises. Properly qualified physicians who wish pediatric training may work in the Clinic to the extent that facilities permit.

A University Children's Clinic has responsibilities and opportunities in many kindred fields of activity. Advancement of knowledge must be fostered and developed, students taught and given guidance, and neighborhood physicians assisted and encouraged. The Clinic must share in the training of nurses and the development of hospital social service. Community contacts and responsibilities in health and social welfare activities must be welcomed. The care and treatment of the children who come to the Clinic must be sympathetically and understandingly given according to the highest standards of current knowledge and with the total situation of child, home, and parents ever in mind. To train young physicians to carry forward these ideals is perhaps the supreme function and opportunity of a Clinic.

For any clinic to live up to its purpose and its opportunities requires, in the words of Francis Peabody, "less of the system and law that kills and more of the spirit that gives life."

Critical Review

VITAMIN D MILK—A RÉSUMÉ

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INTRODUCTION

ADVANCES in our knowledge of vitamins, especially the fat-soluble vitamins, have been outstanding in the realm of nutritional problems. Less than a decade has passed since the first efforts toward augmenting the natural vitamin D content of milk were initiated. During these few years great strides have been made in both the comparatively simple problem of producing what is now termed "vitamin D milk" and in the more complex one of determining to what physical or physicochemical changes this addition to our antirachitic armament owes its potency. The rapidity with which these advances have been made, the never-ending succession of theory evolved, and facts determined, make a complete knowledge, understanding, and proper evaluation of the subject somewhat difficult for the practicing clinician. Consequently, it was felt that a résumé of the work that has led up to our present vitamin D milk and its clinical application might be of value.

Cow's milk, the chief dietary substance of artificially fed infants, has been endowed with a number of virtues by a kind Providence, but it does exhibit a few deficiencies; one of these is a relative lack of the antirachitic factor, vitamin D. Consequently, rickets has always been an extremely common condition in infancy and childhood and even in recent times, in spite of our newer knowledge of nutrition and increasing number of antirachitic medicinal agents, has been and is fairly prevalent due either to the failure to offer antirachitic substances to babies or to the offering of insufficient amounts of these substances Thus, a milk in which the vitamin D content is sufficiently high to afford complete protection against rickets is, a priori, distinctly advantageous inasmuch as it represents an automatic form of prophylactic therapy.

Efforts to augment the natural vitamin D content of cow's milk have thus far included:

I. Direct irradiation of the milk.
II. Feeding of vitamin D concentrates to cows.
III. Irradiation of cows.
IV. Direct addition of vitamin D concentrates to the milk.

I. DIRECT IRRADIATION OF MILK

In 1924, Alfred Hess[1] announced to the American Pediatric Society his discovery that antirachitic properties could be imparted to certain substances by exposure to ultraviolet irradiation. The value of

light rays in the treatment of rickets had suggested to him the problem whether exposure of inert substances to ultraviolet rays could endow them with antirachitic potency. Consequently, various fluids were subjected to irradiation.[2] Cottonseed oil was exposed in a Petri dish for one hour at a distance of one foot from a mercury vapor quartz lamp and was then fed in amounts of 0.1 and 0.25 c.c. daily to rats on a standard rachitic diet. Control animals were given nonirradiated oil. It was found that the oil that had been irradiated acquired properties which protected the rats against rickets while the control animals developed the disease in the usual manner. Similar results were obtained when linseed oil was irradiated. The rats which were protected showed a serum inorganic phosphorus content of 6.84 milligrams per cent in comparison with 3.22 milligrams per cent in the rachitic controls. Irradiated mineral oil, in contradistinction to cottonseed and linseed oil, failed to offer any protection. At that time, Hess felt it was too early to discuss the nature of the change brought about in these fluids which imparted to them the antirachitic potency.

Hess[3, 4] then proceeded to investigate whether the same results could be obtained in growing plants, whether similar differences could be demonstrated between vegetables and plants grown in the dark and those grown in the light and subjected to irradiations from a mercury lamp. These problems were subjected to experimental analysis. Wheat was grown in the laboratory both in darkness and in light with irradiation given daily for one hour. The wheat was then fed to rats, in daily amounts of ten grams, in addition to the routine rachitic diet. The rats receiving the wheat grown in darkness (etiolated) developed rickets while those ingesting the irradiated wheat were protected.

Similarly, and to rule out any rôle or factor that differences in growth might play, ordinary plucked lettuce leaves were irradiated and fed in similar amounts to rats. The same result was obtained as with wheat: the irradiated leaves prevented rickets while the nonirradiated lettuce failed to offer protection. Thus, an antirachitic factor was produced, by irradiation, both in vitro and in the growing plant.

Hess' work was closely followed by that of Steenbock[5, 6] who demonstrated that growth-promoting and bone-calcifying properties could be imparted to rats' rations by exposure to the quartz mercury vapor lamp. When the ration was irradiated at a distance of about two feet for ten minutes, it produced the same effect as when the animals were irradiated directly. This activation took place whether the ration was irradiated in an open dish or in a quartz flask but not in a brown glass bottle. The potency was not subsequently destroyed by subjecting the food to a vacuum, heating at 96° C. for forty-five minutes or allowing to stand for twenty-four hours. (It was later demonstrated that irradiated olive oil could stand for ten months without losing its potency[7].) The previous observations of Goldblatt and Soames were also confirmed when it was demonstrated by feeding experiments that tissue such as lung, liver, or muscle taken from directly irradiated animals had antirachitic properties. Furthermore, such tissue could also be endowed directly with growth-promoting and bone-calcifying properties by exposure to ultraviolet light. Protection against rickets in the animals receiving the irradiated substances was not only judged by clinical standards but was confirmed by histologic sections[8] and by chemical analysis of bones. The femora of control animals showed

an average ash content of 47.2 per cent while those of the animals receiving irradiated rations had an average ash content of 53.9 per cent.[6]

The number of substances capable of activation by irradiation was further amplified and included such diverse materials as:[9, 10, 11] vegetable oils, wheat, corn, flour, yeast, egg yolk, butter, plants and vegetables, animal tissues, and what is of especial interest for our immediate discussion, milk. Thus a firm foundation was laid for further experimental and clinical work.

The knowledge that experimental animals could be protected against and cured of rickets by the ingestion of irradiated food, including milk, was soon put to clinical application. Cowell[12] was probably the first to give a clinical report on the feeding of irradiated milk to infants. Three young children, from one and a half to two and a half years of age, with active rickets were the first human subjects. They were given a diet whose only antirachitic value lay in the daily ingestion of a pint of milk. The two infants who received irradiated milk (exposed for twenty minutes at a distance of three feet from a mercury vapor lamp) showed definite improvement at the end of four weeks. The third infant, who acted as a control and received nonirradiated milk, showed no change. Kramer[13] followed shortly thereafter with another more careful clinical analysis. Irradiated milk was given to eight rachitic infants. Kramer's method of irradiation consisted of pouring the milk into a large shallow dish and irradiating with a mercury vapor lamp at a distance of two feet for not more than two hours. He felt then, however, that the time was probably excessive and could be reduced to ten or twenty minutes! (This emphasizes the differences in technic of irradiation of a few years ago and of the present day which will be discussed shortly.) In the children receiving the irradiated milk, healing of rickets was demonstrable by the third week and was usually well marked by the fourth week. The phosphorus content of the blood was raised, reaching a normal level about the fourth week of treatment. Control patients, who were on the same diet save for lack of activation of the milk, showed no improvement. György[14] gave the first German report on the efficacy of irradiated milk in the treatment of rickets. Irradiated milk was given to eighteen children with florid rickets with marked improvement in sixteen, judging by clinical, blood, and x-ray findings.

Some of the more important references to articles that followed later are appended.[15-35] Most of the reports attested to both the prophylactic and curative efficacy of irradiated milk although many investigators found it to be a somewhat slower curative agent than viosterol.[36-38] In Germany, especially, due to the naturally low vitamin D content of the milk produced there, a good deal of investigative work has been done with this antirachitic agent and an abundance of clinical reports has emanated from that country.

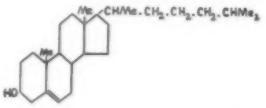
With the clinical value of this type of milk definitely established, further advances in this country have consisted chiefly in improving methods of irradiation. Much of this work has been done by Supplee and his associates.[39-42] A full analysis of the physics, energy quotients, and mechanical difficulties involved would be unnecessary for a medical discussion. Suffice it to say that the wave lengths of the rays which have proved efficient in the irradiation of milk and other substances are of

the magnitude of 300 $\mu\mu$ or 3,000 Å. Rays above 313 $\mu\mu$ in length are of practically no value. It makes but little difference whether the source of the ultraviolet rays is in the form of an arc (such as carbon or magnesium) lamp or a quartz mercury vapor lamp provided comparable amounts of energy are used. Supplee has shown that the degree of antirachitic potency imparted to the milk bears a direct relationship to the amount of energy (in ergs) applied up to a certain limit, beyond which further increases in energy applied increase the vitamin D content but little. The efficiency of the reaction is probably greatest during the first few seconds of exposure. The present method of irradiation consists of uniformly exposing the milk in the form of a moving film which receives rays from carbon arc lamps at constantly changing angles of incidence, varying from 0 to 90°. The thickness of the film of milk is about 0.4 mm. and the time of exposure does not exceed sixteen seconds. Each cubic centimeter of milk receives about two and one-half million ergs of radiant energy. The resulting formation of vitamin D represents a large percentage of the maximum obtainable, yet the exposure is so short as not to cause detectable changes in taste or smell or vitamin A content. Scholl, in Germany, has devised a system of irradiating the milk in the presence of an atmosphere of carbonic acid gas, in order to avoid changes in taste and smell, but with the present short exposure, this seems unnecessary.

What chemical, physical, or physicochemical changes are brought about by the irradiation of milk or other substances that enable them to assume antirachitic properties? How can we correlate two such utterly different factors as vitamin D and ultraviolet rays? The answers to these questions, while not as yet fully complete, have been built up on a series of painstaking experiments evaluated by the clear logic of several brilliant workers.

It may be recalled that Hess in his early experiments was able to endow a large number of seemingly heterogeneous substances with antirachitic powers. The question immediately arose whether the irradiation per se was the prime factor in the activation. It was known that ozone was formed when the ultraviolet lamps were used and in order to rule out this substance as the causative agent of antirachitic potency, ozonated water was fed to rachitic rats. There was no improvement in their condition. Similarly, hydrogen peroxide might be formed but it, too, was found to be devoid of any antirachitic value. It was then shown, by fractionization of vegetable oils, as Zucker[43] had previously demonstrated in cod liver oil, that the active irradiable principle was present only in the nonsaponifiable portion of the oil.[44] This principle was shown to be a sterol, presumably cholesterol. Rosenheim and Webster[45] also found that cholesterol could be activated and endowed with antirachitic properties. Substances rich in cholesterol, such as skin, could be rendered highly antirachitic.[10, 46] That the resulting change was probably a simple chemical or physicochemical one rather than a complex biologic process was attested to by the fact that detached skin, obviously entirely deprived of connection with nervous or circulatory system, could be irradiated and rendered antirachitic.[11] In the plant world, where there is no cholesterol, it was demonstrated that the sterol, corresponding to cholesterol in the animal kingdom, is phytosterol.

Cholesterol, it seemed then, was the primary substance which in some way was changed during the process of irradiation and, with this metamorphosis, assumed antirachitic properties. Cholesterol, it may be stated, is an optically active unsaturated sterol whose structural formula, while not definitely settled, is probably represented by:[47]



Of particular interest is the presence of the hydroxyl group and the double bond between two carbon atoms. The presence of both of these has been shown to be necessary for activation by irradiation. Thus, compounds in which the double bond is saturated by hydrogenation, i.e., dihydrosterol cannot be activated.[10, 48, 49] Nor can compounds in which the hydroxyl group is replaced by other groups, i.e., cholesterol chloride,[50] be activated. (Strictly speaking, this is not absolutely true as the esters of cholesterol, such as cholesterol acetate, have been activated, but this is probably due to the fact that the esters are very easily hydrolyzed, thus restoring the hydroxyl group.[51, 52])

However, the work was still by no means completed. It was found by Hess and Windaus[53] and Rosenheim and Webster[52, 54] that highly purified cholesterol lost its power of assuming antirachitic activity on irradiation. They felt, then, that there was some contaminating substance closely associated with cholesterol to which the latter owes its activity. This had been previously suspected by Zucker[43] and by Steenbock.[9] It was found that when this contaminating substance was separated and irradiated, it had a potency at least 500 times that of irradiated cholesterol.[55] In the meantime, Hess and Windaus, experimenting with a large number of cholesterol derivatives, found that only ergosterol was capable of being rendered antirachitic by irradiation.[56, 57]

As may be suspected, the contaminating substance intimately associated with cholesterol and ergosterol are one and the same. It seems at present that ergosterol is the only substance capable of assuming antirachitic properties during the process of irradiation. All substances owe their power of becoming antirachitic following irradiation to the contaminating presence, in minute quantities, of ergosterol, which apparently is the precursor of vitamin D.

Ergosterol is a sterol closely related to cholesterol but containing three unsaturated double bonds and may probably be represented by the formula:[47, 58]

Exactly what happens during the process of irradiation is not yet definitely known. Oxidative changes are ruled out by the fact that irradiation is equally successful in producing antirachitic potency in an atmosphere of nitrogen. Probably no chemical change per se takes

place as following irradiation, the melting point, optical rotation, and composition according to analysis remain unaltered.[59] There has, however, been demonstrated a definite alteration in spectral absorption.[60, 61, 62] Hess[63] felt that some isometric change took place on irradiation. Wejdling,[64] believing that the crystalline structure of ergosterol might be changed in the process of activation, felt that the change should be demonstrable by measuring the change in the distance between atoms *in vacuo* by means of x-rays. He found, instead, that at the moment of strongest activation no crystalline structure was left, that as soon as ergosterol was transformed by irradiation into the vitamin, the atoms lost their regular arrangement. This may explain why once the substance is overexposed to ultraviolet irradiation it loses its activity and can never be reactivated.

To recapitulate: substances, including milk, which can be rendered antirachitic by irradiation owe this property to the presence of varying contaminating amounts of ergosterol, which is the forerunner of vitamin D. It is the only substance which has thus far been definitely shown to be capable of activation. Precisely what physical or physicochemical change takes place on irradiation is not yet known.

II. FEEDING OF VITAMIN D CONCENTRATES TO COWS—"YEAST" MILK

In the early stages of the work on vitamins, Funk advanced the suggestion that the secretion of these factors in milk was controlled by their presence in the food of the lactating animal. However, it was not until a number of years had passed before attempts were made to increase the vitamin D content of cow's milk by the addition of large amounts of vitamin D to the cow's diet.

In 1924, Lesné and Vigliano[65] added 500 gm. of cod liver oil daily to a cow's feed. When tested experimentally, the milk produced showed increased antirachitic potency, exhibiting good curative and protective powers against rickets. The following year, Wagner[66] could demonstrate no increase in the antirachitic potency of milk of cows fed from 50 to 300 gm. of cod liver oil daily. Golding et al.,[67] however, felt that the addition of 8 ounces of cod liver oil daily to a cow's winter ration did raise the antirachitic potency somewhat. The addition of 2 ounces daily had no demonstrable effect.[68] Failure to increase the vitamin D content of cow's milk by the addition of cod liver oil to the feed may well be explained by the fact that such large doses as are necessary decrease markedly the fat moiety of the milk in which the antirachitic factor lies.

Similar experiments were being conducted about the same time on humans. Hess fed cod liver oil to both pregnant and lactating women in an attempt to supply additional vitamin D to the young. The results were disappointing and Hess concluded that rickets in the offspring could not be prevented by improving the mother's diets either during pregnancy or lactation.[69, 70] Weech[71] performed a similar experiment on a group of lactating mothers (colored) and thought that while the administration of cod liver oil to the lactating mother is not a satisfactory method of preventing rickets in the young, a certain amount of additional antirachitic substance does pass into the milk, effecting a rise in the serum calcium-phosphorus product in the infant and lessening x-ray evidences of the disease. Gerstenberger's[72] efforts to increase the vitamin D content of the milk of wet-nurses by

feeding them a half ounce of cod liver oil daily resulted in failure. Thus we see that the addition of vitamin D in the form of cod liver oil to the diet of lactating animals—both bovine and human—proved, on the whole, unsuccessful.

However, with the introduction, within a few years, of such highly potent vitamin D concentrates as irradiated ergosterol and irradiated yeast, success seemed more imminent. Eufinger et al.[73] were the first to increase satisfactorily the vitamin D content of human milk by feeding vigantol (irradiated ergosterol) to lactating mothers. After only a few days of this supplementary feeding, both the colostrum and milk became highly antirachitic. Similarly, Gerstenberger[74] gave 15 mg. of irradiated ergosterol daily to wet-nurses. Rachitic infants who received from one pint to one quart of this milk daily showed rapid healing. He felt that a daily dose to lactating mothers of from 2 to 3 mg. of irradiated ergosterol would be adequate to give their milk good antirachitic properties.

Wachtel[75] was the first to feed irradiated yeast to cows and thereby markedly increase the vitamin D content of the milk produced. His work was closely followed by the investigations of Steenbock and his coworkers.[76] Steenbock fed 200 gm. of irradiated yeast daily to cows. The milk produced showed high antirachitic potency as measured by feeding experiments with rats. While the femora of groups of rats on ordinary milk showed an average ash content of from 34 to 37 per cent, the bones of the animals on "yeast" milk showed an ash content of 52 per cent, demonstrating the marked calcifying properties of the "yeast" milk. When the daily amount of irradiated yeast was reduced to 10 gm., the resulting butter fat of the milk produced was naturally much less calcifying but was still superior to the butter fat produced on an unsupplemented diet. Steenbock felt that this amount of irradiated yeast produced about the same effect as the daily ingestion of 6 ounces of cod liver oil.

Thomas and MacLeod[77] conducted similar experiments on twenty-one cows divided into seven groups. One group was left on an unsupplemented diet as a control; the next three groups were given, respectively, 10,000, 30,000, and 60,000 rat units of vitamin D in the form of irradiated yeast; and the last three groups were fed 15,000, 45,000, and 135,000 rat units of vitamin D in the form of irradiated ergosterol. The butter fats of their milks were then compared by feeding to rats on a rachitic diet and the antirachitic potencies measured by the line test. The relative potencies of the butter fats are shown in Table I.

TABLE I

RAT UNITS FED	RELATIVE ANTIRACHITIC POTENCY OF BUTTER FAT
Control	1
10,000 units as irradiated yeast	2
30,000 units as irradiated yeast	8
60,000 units as irradiated yeast	16
15,000 units as irradiated ergosterol	2
45,000 units as irradiated ergosterol	4
135,000 units as irradiated ergosterol	16

Krauss', Bethke's, and Monroe's[78] experience, with irradiated ergosterol only, proved to be similar. A study of the antirachitic poten-

cies of the butter fats of milk produced with increasing administration of irradiated ergosterol showed the following comparative values:

RAT UNITS OF VITAMIN D FED TO COWS DAILY	CRITICAL DAILY LEVEL OF B. F. (TO PRODUCE DEFINITE EVIDENCES OF HEALING IN THE RAT)	RAT UNITS PER GM. OF B. F.
0	600 mg.	0.17
7,500	350 mg.	0.29
15,000	200 mg.	0.50
100,000	60 mg.	1.67
200,000	40 mg.	2.50

Thus, we see that according to their figures, the antirachitic potency was increased approximately fifteen times by the daily administration of 200,000 units of vitamin D as irradiated ergosterol. Judging from Thomas and MacLeod's results and those of Hardenbergh and Wilson,[79] which follow shortly, these are really rather conservative increases.

The latter investigators fed irradiated yeast and irradiated ergosterol as supplementary vitamin D offerings. The ergosterol was fed in daily amounts of 100,000 and 200,000 rat units and the yeast in daily amounts of 30,000 and 60,000 rat units with the comparative increases in antirachitic potency as shown in Table II.

TABLE II

SUPPLEMENT FED	RAT UNITS OF VITAMIN D FED DAILY	AMOUNT OF B. F. CONTAINING 1 RAT UNIT	RELATIVE POTENCIES
Control	------	8.0 gm.	1
Irradiated ergosterol	100,000	0.5 gm.	16
Irradiated ergosterol	200,000	0.25 gm.	32
Irradiated yeast	30,000	0.5 gm.	16
Irradiated yeast	60,000	0.25 gm.	32

Irradiated yeast seems to be the supplement of choice as it has proved to be about three times as effective as irradiated ergosterol on the basis of the number of rat units fed.

Clinical experiences with yeast milk (including in this term milk produced with either yeast or ergosterol supplements) have, with rare exception, been excellent although Gerstenberger's[80] report on the clinical use of the milk produced in Krauss' feeding experiments seemed somewhat disappointing. Two rachitic infants who were given one pint of this milk daily (plus one pint of ordinary skimmed milk and sufficient carbohydrate to meet their caloric needs) showed rather slow healing. The bones of the two infants were not completely healed at the end of ten and eleven weeks, respectively; the blood calcium levels became normal only after the tenth week, and the serum phosphorus had not attained a normal value by the end of the experiment. Gerstenberger felt, from comparative clinical experience with cod liver oil, that a pint of this fortified milk contained slightly less than half a teaspoonful of cod liver oil equivalence.

Other reports have definitely shown this milk to have excellent protective and curative powers. Hess and his coworkers[81] reported clini-

cal results on a group of 102 infants, many of them colored or Italian, who were given milk from cows fed 100,000 and 200,000 units of ergosterol and 30,000 and 60,000 units of irradiated yeast. This milk, as we have seen, is sixteen and thirty-two times as potent as ordinary milk, and assays 80 and 160 units of vitamin D, respectively, to the quart. All but the weaker yeast milk proved quite satisfactory from both the curative and protective standpoint. Two reports by Wyman[82, 83] have been quite favorable. Kramer's and Gittleman's[84] experience with the use of a yeast milk treated so as to contain only 55 and 40 units, respectively, of vitamin D was eminently satisfactory from the curative standpoint.

III. IRRADIATION OF COWS

The efficacy of exposure of the lactating animal to light rays as a means of increasing the vitamin D content of its milk has been both opposed and upheld. Luce[85, 86] was one of the first to investigate the relative influence of diet and exposure to sunlight on the growth-promoting and antirachitic properties of milk produced by cattle. She found that milk from pasture-fed cattle had a definitely higher antirachitic value than milk from cows that were stall-fed in the dark. However, it was found impossible, by means of sunlight alone, to raise the antirachitic value of the milk if the diet of the cows was deficient. She concluded, therefore, that exposure to sunlight plays only a minor, subsidiary rôle in the production of vitamin D factors in the milk. Chick and Roscoe,[87] however, expressed the opinion, following experimental work, that while the diet was the important factor in the production of vitamin A, the degree of insolation played the more important rôle in the determination of the antirachitic potency of the milk produced. Supplee and Dow[88] found that summer milk contained somewhat higher amounts of vitamin D than winter milk. Again, it is difficult to evaluate the rôle played by the amount of sunlight and the type of food ingested during these two seasons. However, none of these opinions are of much aid in determining the extent of increase of vitamin D that might be expected from direct irradiation of the animal by means of a mercury vapor or carbon arc lamp, inasmuch as the sun's rays when they strike the earth are of but meager potency in the ultraviolet range.

Steenbock[89] proceeded to irradiate an animal directly and used for this purpose a lactating goat. The hair was clipped closely, and the animal was irradiated daily. It was found that, while previously a daily ingestion of 12 c.c. of its milk was necessary to cause incipient calcium deposit in experimental animals, following irradiation (as early as four days after irradiation was begun) only 2 c.c. were required to produce the same effect.

Later and similar experiments with cows, however, produced entirely negative results.[90] Cows were exposed daily for one hour at a distance of from 20 to 30 inches from quartz mercury vapor lamps, various regions such as head, back, and udders being irradiated. No demonstrable increase in the vitamin D content of the milk was obtained. We are at a loss to explain this negative result as practically all other investigators have been able to effect an increase in the antirachitic potency of the milk by direct irradiation of the lactating ani-

mal. Thus, Gowen et al.[91] reported that definite curative powers were imparted to cow's milk by exposure of the animal's back to the ultraviolet lamp for as short a period as fifteen or thirty minutes daily. Falkenheim[92] was also successful in raising the vitamin D content by means of direct irradiation of the animal. Wagner and his coworkers[93] irradiated cows daily for one hour at a distance of 50 cm. from the ultraviolet lamp. The milk thus produced was given to eight infants, six of whom were entirely protected against rickets and two, a pair of twins, began to show early craniotabes at the end of three months. It was felt that the milk was satisfactory for ordinary routine prophylaxis against rickets.

Attempts to raise the vitamin D content of breast milk by irradiation of the lactating mother have also proved successful. Hess[94] irradiated a lactating woman every other day for a month. Previously, 25 c.c. of her milk fed to rachitic rats daily had failed to cause any improvement in their condition. Following irradiation, the same quantity of milk caused definite improvement and raised the phosphorus content of the blood of experimental animals from an average of 1.98 mg. per 100 c.c. to 5.61 mg. per 100 c.c. (The phosphorus content of the milk itself was not found to be increased.) Hess pointed out that there was an increase in the nonsaponifiable fraction of the milk. Gerstenberger[72] and Lesné and Dreyfus-Sée[95] have reported equally successful experiments.

The latest report on the irradiation of cattle comes from Mitchell and his group.[96] Carbon arc lamps were arranged in the stalls so that each cow's udders were exposed on one side to the lamp for fifteen minutes daily. The lamps were at a distance of about two feet from the animals and were in this order:

Cow: Lamp: Cow: Cow: Lamp: Cow: Cow: Lamp: Cow.

Biologic assay of the milk from irradiated animals showed the antirachitic potency to be approximately 22 rat units of vitamin D per quart as compared with 5 rat units of vitamin D per quart for ordinary milk. Feeding experiments with twenty-one infants over a six- to eight-month period showed that this milk had as good protective powers against rickets as directly irradiated milk.

IV. DIRECT ADDITION OF VITAMIN D CONCENTRATE TO THE MILK

This, the latest, method of increasing the vitamin D potency of cow's milk has been reported by Zucker.[97] A concentrate of cod liver oil of high potency and purity furnished in the form of a "150 D" preparation, i.e., a preparation 150 times as potent as standard cod liver oil as measured by the Steenbock line test, is diluted in the proportion of one part in 12,000 parts of milk. This procedure results in a milk which contains approximately 150 units of vitamin D to the quart or the equivalent of about three teaspoonfuls of cod liver oil. The incorporation of the concentrate can be done by homogenization, partial homogenization, or by a third method not involving homogenization. There is no separation of the concentrate from the cream by any of these methods. The milk has been frequently assayed on rats with excellent results from both the curative and protective standpoint. Investigation by Barnes[98] with the use of the concentrate in infants has shown it to be a highly effective antirachitic agent, effecting, in rachitic infants, a return to normal of the serum calcium and phosphorus and the

x-ray findings within two weeks. One hundred and fifty units of vitamin D per quart has been selected as the amount which has seemed from clinical experience with cod liver oil to be a good prophylactic standard.

DISCUSSION

What should be stressed in a comparison of the relative advantages and disadvantages of these various methods devised for increasing the antirachitic potency of cow's milk?

Earlier objections to directly irradiated milk were largely due to errors of technic in irradiation. Thus such disadvantages as changes in taste and smell and destruction of vitamin A have been shown to be definitely attributable to overexposure to the ultraviolet rays. With the present exposure of only sixteen seconds, there is no detectable change in palatability or vitamin A potency.[99] Supplee and Dow[100] have demonstrated a slight but measurable loss in vitamin C potency in irradiated fluid milk but not in irradiated dried milk. Inasmuch as antiscorbutic factors are added routinely to the infant's diet, this slight loss of vitamin C is of practically no importance. This method, of course, does require additional apparatus and is applicable chiefly to centers with large pasteurizing plants. In smaller communities, the installation of such apparatus would hardly be commercially and financially advisable. However, as irradiated dried milk it may be shipped to all parts of the country and kept for several months without any loss in antirachitic potency.

In its favor is the fact that no special feeding or supervision of cattle is necessary. The milk is shipped as usual into the pasteurizing plant and the additional process of irradiation is easily and quickly performed at a cost of only a fraction of a cent per quart of milk. Any objection to the method because it involves further handling of the milk is met with the answer that far from the introduction of any contaminating process, the irradiation has been actually shown to lower markedly the bacterial count.[25, 101, 102] The milk, following irradiation, has a vitamin D content of approximately 50 to 55 rat units which has seemingly proved ample for both curative and protective purposes.

The production of yeast milk involves special supervision and feeding of cattle and, because it is difficult to follow closely, due to the long experimental work involved, the potency of a milk supply whose vitamin D content is dependent on feeding operations carried on over scattered areas, is at present and probably for the near future limited to supervized dairy farms such as are now able to put certified milk on the market. These farms are, of necessity, limited to areas supplying large urban districts such as New York, Boston, and Philadelphia. At present, the method is a good deal more expensive than the direct irradiation of milk. Krauss feels that the feeding method is a more natural procedure for increasing the vitamin D content of cow's milk. No further handling or treatment of the milk is necessary. No untoward effects on the cattle have been observed with continued feeding of the yeast or ergosterol.

Hess, in a comparison of the two milks, i.e. "yeast" and irradiated, was inclined to place the yeast milk second in point of efficacy because, in clinical experiments, the same results seemed to be obtained with irradiated milk, which contains only about 50 units of vitamin D to the quart as with the yeast milk which contains 160 units of vitamin D

to the quart. However, Kramer[84] has shown that yeast milk treated so as to contain only 55 and 40 units, respectively, of vitamin D to the quart is as efficacious as a curative agent as irradiated milk containing the same number of vitamin D units.

The direct irradiation of animals again involves special apparatus. Once installed, however, the actual process of irradiating an animal for fifteen minutes a day does not seem too involved. Close supervision, as required in supplementary feeding, does not seem necessary. We have again, however, the same objection as with yeast milk, namely, the difficulty in following closely the potency of a milk, whose vitamin D content, in this case, is dependent on irradiation operations carried on over widely scattered areas. A little more clinical evidence as to its efficacy, moreover, seems indicated. The method resulted, according to Mitchell, in a milk having an antirachitic potency of only 22 units of vitamin D per quart, which is only about four times that of ordinary milk. Whether this will be sufficiently protective under all types of circumstances remains to be corroborated.

The fourth method seems very simple and does not depend on special, controlled feeding of cows or on elaborate apparatus. Small pasteurization plants can carry out the procedure equally as well as large ones. The potency of the milk is definitely known beforehand; one does not have to wait for several weeks of animal experimentation to evaluate the potency. The chances for error are minimal as the whole procedure involves only the addition of a standardized, previously assayed concentrate. While the procedure is probably more expensive than direct irradiation of milk, the price nevertheless is less than that of ordinary milk plus cod liver oil. The method does not have to be restricted to larger centers of population but can be used wherever there is a pasteurization plant.

There remains, finally, a question which has as yet not been satisfactorily answered. Hess was one of the first to place it before us. Why are fewer units of vitamin D in the form of vitamin D milk sufficient to protect against rickets than in the form of other antirachitic agents, such as cod liver oil or viosterol? Hess[81] compared the potency of yeast milk with that of cod liver oil and of viosterol in Table III.

TABLE III

INTAKE OF COW IN RAT UNITS		MILK (1 LITER) IN TERMS OF		
		RAT UNITS	VIOSTEROL (DROPS)	COD LIVER OIL (GM.)
Ergosterol	100,000	80	1	6
Ergosterol	200,000	160	2	12
Yeast	30,000	80	1	6
Yeast	60,000	160	2	12

He drew the conclusion that yeast milk is more comparable to cod liver oil than to viosterol, for while 12 gm. of cod liver oil (corresponding to one liter of the 160 D milk) would be a fair daily prophylactic dose for infants, 2 drops of viosterol would be highly inadequate. Hess then further demonstrated that one liter of milk, 15 c.c. of cod liver oil, and 10 drops of viosterol are each sufficient as a daily dose to protect the average infant from rickets. If these figures are transposed into rat units, we find the comparative potencies are: 160:200:830 or in the

ratio of 1:1.25:5.2. The difference between the yeast milk and viosterol is striking, that between the milk and cod liver oil not so pronounced. However, Kramer has shown that as little as 40 units of vitamin D in the form of yeast milk daily is sufficient as a curative agent in rickets. This would make the ratio: 40:200:830 or approximately 1:5:21. Similar results have been recorded for irradiated milk, and numerous clinical reports attest to the efficacy of irradiated milk containing only 50 units of vitamin D per quart. As we have seen, the direct irradiation of cattle results in a milk which contains only 22 units of vitamin D per quart, and yet the milk has seemed to be an efficient protective agent. On reviewing earlier reports, we see that MacKay and Shaw[15, 19] effected healing of rickets in from two to three weeks with as little as 3½ ounces of irradiated dried milk or 5 ounces of irradiated condensed milk daily! This amount of milk probably did not contain even 20 units of vitamin D. Thus, we have extensive clinical evidence to the effect that far fewer units of vitamin D in the form of vitamin D milk are required to protect against or heal rickets than is the case for other antirachitic agents.

Watson[103] has given us an interesting discussion of this problem. He states in part: "According to official biologic tests, the increase in the amount of antirachitic property in milk brought about by irradiation is, from the laboratory point of view, trifling in comparison with the large amount of vitamin D present in various irradiated medicinal substances. On the other hand, we have the striking fact that irradiated milk has been shown to cure rickets in cases which have failed to respond to the prolonged administration of irradiated commercial preparations in common use. What is the explanation of this anomaly? It is possible that irradiated medicinal substances may steadily lose their curative powers, milk having the advantage of being consumed in the fresh state. It is equally possible that irradiated milk possesses some property of value which is not determined by the present laboratory test for vitamin D. There is the further possibility of a tendency to err in thinking the results obtained from experiments in rats under laboratory conditions are capable of fairly rigid application to clinical conditions in the human subject. It is conceivable that the milk acts merely as a carrier of some specific energy imparted to it by suitable irradiation, this added property only coming into action in the tissues. In this event, it would be clear that its action is not the same as in the case of irradiated ergosterol where a definite physical change is effected in the ergosterol by the irradiation process." Watson believes we must come to the conclusion that some vital property has been added to the milk which is not represented by the present laboratory test for vitamin D. He proceeds: "In nature, vitamins are found only in the vegetable kingdom. Vitamins in animal tissues and in milk are derived from the vegetable foods consumed. The vital energy of the sun strikes the cells in the plant, and in those cells the solar energy is transformed into a chemical vital energy which promotes the normal growth and development of the tissues in the vegetable kingdom. The activated tissues hold some of the original vital energy which initiated the chemical changes. Those tissues are in turn consumed by animals or man, to whom that energy is in turn transmitted as a so-called vitamin. . . . Thus solar energy is transformed in nature and by artificial means (ultraviolet lamp) into chemical energy. It is apparent that between the

chemical energy, as it is stored up in the plant or substance, and the sunlight energy, which starts the process, there must exist a very close kinship in nature, if not indeed identity."

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American Academy of Pediatrics

Proceedings

THIRD ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

MONDAY AFTERNOON SESSION
JUNE 12, 1933

Round Table Conference on Upper Respiratory Infections

Leader: Dr. Isaac A. Abt, Chicago, Ill. Assistant: Dr. Horton R. Casparis, Nashville, Tenn.

DR. ISAAC A. ABT (CHICAGO, ILL.).—Diseases of the upper respiratory tract are among the most frequent affections in children. This group of disorders occurs most commonly during the autumn, winter, and spring. Every practitioner has observed that in some instances colds spread through an entire family. Frequently they will affect many of the children in a classroom, or spread through the entire school. In an infant asylum or in a babies' ward of the hospital, infections of the upper respiratory tract with pulmonary complications may cause an alarming, if not fatal, epidemic. Rachitic, allergic, as well as children of the so-called lymphatic type, are most frequently affected. In many of the infants and children predisposed to catarrhal affections, there seems to exist an indefinable, and not thoroughly understood, constitutional factor.

In addition to this, there are variable external factors such as temperature, air pressure, variations in moisture, as well as in quantity and quality of solar rays. The intensity of the latter fluctuates at different seasons as well as in different geographic locations. It is well known that the ultraviolet radiation reaches its maximum during the summer and its minimum in the winter and that the intensity is greater in the autumn than in the spring.

THE COMMON COLD

The common cold has received the attention of medical men throughout the ages. The affections considered under this classification have been thought to be due to the effect of cold air on the surface of the body during a longer or shorter period. In a more restricted sense it was thought that the effect of cold air on the respiratory tract was capable of producing inflammatory reactions. With the discovery of microorganisms, the infectious nature of the diseases of the upper, as well as the lower respiratory tract, had its vogue, and the old notion of the effect of cold was discarded for a time at least. It is readily conceivable, however, that cold air of itself may produce local effects on skin and mucous membranes, and these effects are to be observed in the narrowing of the superficial vessels with subsequent dilation and congestive phenomena. We have only to think of local frost-bites which are associated with marked inflammation without the presence of microorganisms. A sensitive child whose feet become chilled or wet will very frequently develop tickling in his nose with profuse discharge, and if this manifestation recurs, after repeated exposure of a similar nature, one may feel reasonably certain that there

is a relationship between the cause, wet feet, and the nasopharyngeal catarrh. Though modern authorities consider the cooling of the body a predisposing factor in a nonresistant individual, infection of some kind or another is the exciting cause. To show that cold of itself does not necessarily tend to produce the upper respiratory diseases, is elucidated by the experience of Nansen, the Polar explorer, whose men were exposed to the most severe cold in the Arctic.

None developed any catarrhal symptoms under these conditions. However, on returning to a more populated region many suffered from colds, coughing, and sneezing.

It has been suggested by De Rudder that certain meteorologic conditions affect the autonomic nervous system in such a way as to produce capillary contraction with subsequent local and internal hyperemia. But this assumption is altogether speculative and without further proof remains untenable.

In a recent paper by Dochez, Catherine C. Mills, and Yale Kneeland in the *Journal of the American Medical Association*, the etiology of the diseases of the upper respiratory tract are critically reviewed. These authors consider, in some detail, the organisms which have been thought to be etiologic factors in the production of the common cold. They point out that there is a "basal flora" of the upper respiratory tract composed of organisms which are generally thought to be nonpathogenic and of others that are supposed to be highly pathogenic. The presence of such organisms does not necessarily produce symptoms of infection of the upper respiratory tract. Indeed, even when the infection is in progress, these organisms may not be increased in number. When secondary inflammatory processes of the upper respiratory tract occur, the organisms may be shown to have increased in activity.

They have studied upper respiratory infections in infants and have found that the tract is sterile at birth. The basal flora which is comparable to that of adults, is not acquired until some weeks after birth, yet this transformation from the sterile to the bacteria laden respiratory tract does not necessarily usher in disease.

The authors point out that the common cold occurs in a great proportion of infants who live in institutions, though the basal flora of these infants is not changed. Colds which occur in the early autumn are usually mild, and Dochez and his workers assume that the agent which produces these colds prepares the soil for the dissemination of bacteria. In the midwinter the infections are of a severer type, and pathogenic organisms are thought to play a more important part in the colds and other complications. Thus they point out that there seem to be two types of causal agents: the one which initiates and gives rise to a mild disturbance, and the other, one of the group of pathogenic bacteria, which are now enabled to invade the soil prepared by the initiating agent and give rise to severe secondary manifestations.

FILTRABLE VIRUSES

The authors point out that chimpanzees are susceptible to colds when they are inoculated intranasally with bacteria-free filtrates of nasal washings obtained from early cases of the common cold. Dochez and his workers also point out that following the animal inoculation of these bacteria-free filtrates, certain pathogenic bacteria come to invade the nose and throats of these animals, suggesting that the filtrable viruses prepare a favorable soil in the respiratory tract for the secondary invasion of some of the familiar pathogenic organisms. It is presumptive that the filtrable virus, in the case of common colds, gains access to the upper respiratory tract of human beings and experimental animals, and is capable of producing the milder symptoms of the common cold, which may become more severe, if pathogenic organisms produce secondary infections.

ACID-BASE EQUILIBRIUM

Much has been written recently of the relationship of body chemistry to the upper respiratory diseases. Czerny, in his early writings, mentions the fact that exceedingly large tonsils and adenoids are observed in children who have been fed milk and eggs excessively and for a long period. He says also that in those infants whom he considers to be suffering from exudative diathesis, he recommends an early use of a mixed diet with a decrease in the amount of milk. On the other hand, he begins the use of small quantities of meat early. Finally, he believes that overfeeding during the first year or two of life tends to produce hypertrophy of the tonsils and the lymphoid tissue of the nasopharynx. Weigert believed that retention of water in the body diminished resistance against infection.

Ludwig Meyer in a recent publication, expressed the opinion that the resistance of the nasopharyngeal mucosa against infection may be increased by the use of a rational diet. Food which is low in salt and proteins tends to diminish the water content of the tissues and increases their resistance against infection.

Somewhat along the same line, Stolte maintains that infection is more important than exposure to cold in the upper respiratory diseases though he admits that a rapid loss of heat from the body may predispose to catarrhal disease.

He thinks that catarrhal affections of the upper respiratory tract occur most frequently in the spring after bright, sunny warm days; that the sudden application of sunlight affects the body by increasing the magnesium and potassium content of the blood and decreasing its calcium. As a result of these changes he believes the water content of the tissues is increased, thus diminishing resistance and producing a greater susceptibility to upper respiratory infections.

The writings of D. C. Jarvis of Barre, Vermont, and his associates have attracted widespread attention. Jarvis observed that acid-producing food represented the greater part of American dietary. Under this dietary regime he noticed an increase in the redness of the mucous membrane covering the cartilaginous portion of the nasal septum, and often to a lesser degree an increase in redness of the mucous membrane covering the anterior pillars of the fauces and the aryepiglottic folds. On the other hand, in individuals selecting most of their food from alkaline diets, there was an absence of this redness in the locations mentioned above. In the patients with the red nasal septum, alkaline dietetic treatment was employed using primarily the citrus fruits. Jarvis also found that excessive sweets in the diet produced redness of the turbinates and subacute laryngitis and that a catarrhal discharge from the nose and throat was observed when there was a lack of the proper amount of vegetables in the diet. A granular condition of the posterior pharyngeal wall was observed when there was an excess of foods made from flour. Finally, the amount of lymphoid tissue was increased when there was insufficient fat in the diet. By correcting the diets in these various patients, marked improvement occurred.

Some control observations were recently made by Bernheimer and Cohen, who could not corroborate Jarvis' findings. There is some clinical evidence extending over a considerable period of time which indicates there may be a relationship between diet and catarrhal conditions of the upper respiratory tract.

VITAMINS

Recent work seems to indicate that vitamins A and D seem to offer no protection against the occurrence of respiratory diseases. It has also been found that the exposure to ultraviolet rays does not seem to diminish the occurrence of colds in the light-treated groups. The investigators at Johns Hopkins University have also pointed out that neither abnormalities of the upper air passages nor hygienic sleep-

ing conditions, clothing, exercise, habits, and other commonly assigned causes increase either the susceptibility or the resistance to infection of the upper respiratory tract.

ALLERGY IN UPPER RESPIRATORY INFECTIONS

The allergic diseases of the upper respiratory tract frequently seem to have an hereditary background. In a large number of infants and children with allergic manifestations, a family history of anaphylactic reactions is obtained. Sometimes one parent and at other times both are affected.

Longcope has attempted to explain the nature of allergy in some children by saying that it may be caused by the inherited quality of tissue which too readily builds up what may be termed a selective hypersensitiveness. It has also been stated that sensitization may be developed during intercurrent disease possibly due to the absorption of bacterial proteins or to overindulgence in certain foods. Sensitization to eggs may be observed for the first time during an acute illness.

The nature of the allergic diathesis is not understood, despite physicochemical researches. It is not necessary to mention the various vegetable and animal agents, not excluding house dust, which are found to produce allergic reactions. Hay fever, asthma, and allied manifestations may occur in infants and children of every age. One sometimes observes a recurrent bronchitis or asthma associated with eczema during the first year of life. In examination of a given case of hay fever, it is of value to determine whether the vasomotor symptoms are actually excited by the pollen of plants or whether they arise from other causes. Goodale believes that a fairly large proportion of patients who come under his observation show no response to pollens, but the nasal response seems to be excited by the fragrance of the flowers such as lilies of the valley, lilacs, and other flowering plants. Olfactory, vasomotor rhinitis or pseudohay fever may be caused by mechanical, thermal, chemical, and odorific irritants, in addition to the protein substances, both animal and vegetable, already mentioned.

Duke believes that certain of the upper respiratory affections originate through a disorder in the heat regulating mechanism. He believes that many of the noninfectious coryzas, asthmas, as well as dermatoses have their origin during or following the onset of an acute disease. Certain persons may become abnormally sensitive to heat or cold. Duke speaks of thermic coryza, thermic asthma or thermic urticaria or eczema; also of heat sensitive and cold sensitive patients. The nasal symptoms produced are manifested by sneezing, swelling of the mucous membranes of the nose with the increased secretion of clear mucus. The bronchial symptoms are manifested by cough or asthma with the expectoration of clear mucus. Infection and chronic changes in the mucous membranes may be superimposed upon these conditions. Thus, Duke has introduced a new conception into the nosology of upper respiratory infections, which may in some way explain our age old conception of the relationship of cold to these disorders.

It may be emphasized that many of the acute respiratory affections during infancy and early childhood occur during the fall and winter months and seem to depend on various factors. There may be some source of infection in the child's environment and also a particular susceptibility indicating his degree of nonimmunity. In the winter the child comes in more intimate contact with other members of the household or institution in which he lives than during the summer, hence the greater frequency of colds during the winter. The immunity of the child is lower during the winter than during the summer, possibly because he has less opportunity for exposure to the sunshine and, as has been claimed by some, a diminished vitamin content in his food. The young patients are affected in large numbers, especially

if after a period of warm, fine weather there is a sudden fall of temperature with a decline of atmospheric pressure and an increase in the velocity of the wind with a dust-laden atmosphere.

COURSE OF THE AFFECTION

In the catarrhal states of the upper respiratory tract, one observes marked hyperemia of the mucous membranes with an increase of secretion and round-cell infiltration of the mucous and submucous coats. The infiltration is most marked around the vessels and the dilated excretory ducts of the glands. During the height of the disease there is a marked swollen, reddened, moist mucous membrane which produces a thin secretion with considerable mucus. Gradually this secretion becomes thick and purulent in character, due to the admixture of epithelial cells and leucocytes. This process tends to recede and after a course of two or three weeks the inflammation has subsided and the secretion has disappeared.

At times the acute respiratory affections are preceded by several days of constitutional disturbances such as malaise, moderate headache, slight elevation of temperature, sneezing, burning sensation in the throat, moderate hoarseness, feeling of dryness in the pharynx, and the changes in the mucosa which have already been described. These catarrhal changes may involve the mucous membrane of the upper respiratory tract from the nose to the bronchi. The infectious agent, whatever it is, may spread along the mucous membrane or in the submucous tissue and involve a considerable extent of surface. The nasal involvement is characterized by obstruction and discharge. The face may be puffy, the eyes red and secreting, and the upper lip swollen. The child breathes with his mouth open, and there is a fetor to his breath. The child is restless at night, sleeps poorly, and snores. In the young infant the temperature may be as high as 104° F., and the infant has difficulty in taking the bottle or the breast. At times he becomes dyspneic. The abdomen may become tympanitic, or convulsions may occur, or the finer bronchi may be involved, terminating in bronchopneumonia.

In the older child the condition may become protracted, and during the acute stage he may complain of a headache. In most of these cases an involvement of the nasal accessory sinuses has occurred. Sometimes neuralgia in the region of the supraorbital nerves causes discomfort. Epistaxis, preceded by continuous or violent sneezing, has been caused by rupture of a small vessel in the septum. The coryza may cause disturbances in the sense of smell, as well as in the sense of taste, which may lead to loss of appetite and refusal of food. An associated inflammation is usually present in the nasopharynx. The eustachian tube becomes swollen, consequently the hearing is diminished or the infection may be carried to the middle ear, producing an otitis media. The severity of the disease varies with the age of the patient. Young infants may become alarmingly sick while older children may run the course of a mild local infection.

The retropharyngeal, and the submaxillary lymph glands are frequently swollen, or they may suppurate. The catarrhal process may extend to the larynx and trachea and produce dryness with a hoarse voice and dry irritating cough, which may be accompanied in older children with some mucopurulent discharge, or the mucosa of the larynx may be red and swollen with extreme dryness. A thick tenacious secretion covers the mucosa of the larynx and produces a spasmodic irritating cough. The same condition may occur in the trachea. In extreme cases the laryngitis may increase with the occurrence of edema leading to stridor, barking cough or laryngeal stenosis.

THE ACCESSORY SINUSES

On account of the difficulties in diagnosis, these affections were for a long time disregarded or not recognized. It is known at present that the ethmoidal sinus is

developed during the eighth fetal month and is small, though present, at birth. The maxillary sinuses, while they are developed during the fourth fetal month, are very small at birth. The frontal sinuses are developed from the first to the third year of life and do not become the site of infection until the sixth or seventh year of life. The sphenoidal sinuses develop toward the end of the first year of life and do not become involved until the sixth or seventh year.

If a profuse discharge persists after an acute rhinitis, particularly if the discharge is unilateral, and if one excludes the presence of a foreign body in the nostril, it may be assumed with a considerable degree of certainty that there is an acute involvement of one of the accessory sinuses. In infants this condition is usually confined to one of the ethmoidal sinuses. In infants suffering from ethmoidal involvement, there may be a moderate edema of the eyelid which may be unilateral or bilateral, and in severe cases an abscess of the lid may occur. The simple edema tends to disappear after drainage of the ethmoidal cells. The ordinary lid abscess may be incised and drained, though at times more extensive suppuration may occur producing protrusion of the bulb. In older children other sinuses may be involved. The infection of any one of them may lead to changes in the eye, such as swelling and redness or protrusion of the bulb, retrobulbar abscess, even thrombosis of the orbital vessels. Meningitis by extension is always a possible complication.

Finkelstein and others think most cases of suppuration in the mouth, as well as orbital involvement, are due to infections of the tooth germ. In older children, particularly where there is suppuration within the maxillary sinuses, abscesses may form in the neighborhood.

Osteomyelitis of the upper jaw usually occurs in young infants or young children; is rarely observed in children of school age, and is usually recognized because of the orbital involvement, as both upper and lower lids are edematous. These patients usually have high fever, the affected side of the face is swollen, the bulb may protrude, or it may be displaced to one side or the other and abscesses may form in the mouth, the gums of the upper jaw, with the destruction of the rudimentary teeth.

The sinusitis may become chronic, and after the third year of life, these chronic affections may be the cause of ill health. The submucosa may become fibrosed, and epithelial changes may occur on the mucous surface. The chronic sinusitis may lead to protracted nasal catarrh with mucous discharge. In older children with maxillary sinus infection, irrigation will wash out mucous plugs with slight admixture of pus. This procedure offers one of the most reliable methods of diagnosis. X-ray examination also gives valuable diagnostic information.

RELATION OF SINUS INFECTION TO SYSTEMIC DISEASE

A protracted or obscure fever may be due to an unrecognized sinusitis. Or, the infective secretions escaping from the sinuses may produce irritation or inflammation in the respiratory or even in the digestive tract. Sinusitis may be the focus for the occurrence of general sepsis, and it has also been maintained that either acute or chronic sinusitis may be the focus for the production of rheumatism, endocarditis, asthma and bronchitis, nephritis, and other remote infections.

RETROPHARYNGEAL ABSCESS

The retropharyngeal lymph nodes may become the site of infection and may break down and suppurate, constituting the not infrequent retropharyngeal abscess. It is well known that one must differentiate these abscesses which originate in the lymph nodes of the pharynx from those which arise from caries of the spinal vertebrae. The latter may be recognized by x-ray examination of the spine and the skull bones.

The retropharyngeal abscess which occupies a high position in the pharynx is difficult to recognize at times. Symptoms are often indistinct though nasal stenosis is most common. The children are restless, and anxious, on account of the difficulty in breathing; sleep is disturbed, and the general condition suffers in consequence. Attention is called to this disease by pain on swallowing. The forward projection of the posterior pharyngeal wall is observed early. Perhaps the most reliable method of diagnosis is gentle palpation and the recognition of a fluctuating mass. Retropharyngeal abscess may be dangerous on account of the possible occurrence of a general sepsis and also the gravitation of the pus into the posterior mediastinal space.

GENERAL SEPSIS

What is understood by sepsis? Schottmüller believes that one may term a disease sepsis when a focus has been formed in the body from which either constantly or periodically pathogenic organisms are poured into the circulation and that on account of this invasion subjective and objective disease manifestations are produced. What has been frequently spoken of as pyemia is today called sepsis with metastases. But with sepsis already in progress, it is necessary or desirable that its source or origin be located. Blood culture would seem at first hand to be the most reliable diagnostic method though this frequently fails. A sign of great value is the occurrence of a chill. A chill indicates that organisms are being poured into the blood stream, and the patient is suffering the consequences. The difficulty is, however, that very young infants frequently do not have chills. The diagnosis of sepsis may be easy, or it may present the utmost difficulty. If there is extensive suppuration in the pharynx the way is pointed out. Frequently, however, there are no external signs. The tonsillitis may have entirely disappeared, and it may be ten days or two weeks before the symptoms of sepsis show themselves. A suppurating process in the pharynx or large painful lymph nodes in the neck are of diagnostic importance. The glands in the neck may lie under the sternocleidomastoid muscle and may escape attention. Pain is frequently present in cases of pharyngeal sepsis.

The internal organs in cases of sepsis should be frequently examined. This is particularly true of the heart, lungs, kidneys, as well as the joints. Sometimes the first inkling of the correct diagnosis is obtained from the involvement of more remote organs.

POSTANGINAL SEPSIS

Postanginal sepsis has been infrequently reported in early childhood. A review of this condition was published by the author in the JOURNAL OF PEDIATRICS, July, 1932.

HEMORRHAGE FROM PHARYNGEAL AND PERITONSILLAR ABSCESS

Pharyngitis or tonsillitis, whether occurring as a part of a nonspecific upper respiratory infection or one of the contagious diseases, may lead to suppuration in the adjacent tissues and as a result retropharyngeal and peritonsillar abscesses occur. In retropharyngeal abscess, the infection is carried by lymphatics to small lymph glands lying anterolateral to the upper cervical vertebra which break down, causing an accumulation of pus, which is circumscribed within the pharyngeal limits, but which in some instances may follow the deep fascial planes up to the base of the skull or down to the mediastinum.

Infection of the parapharyngeal spaces is in most instances blood-borne through thrombosed veins leading from the tonsil plexus to the tissues external to the middle constrictor and from there may spread to the submaxillary, carotid sheath, and parotid spaces. The pathways of infection are both lymphatic and venous, as well

as by direct contiguity of tissue, depending on the type of infection. The internal carotid artery lies closer to the pharyngeal wall than the external carotid. The internal carotid artery normally makes several curves in its course in the neck which may become exaggerated into tortuosities that will bring it into close proximity to the pharyngeal mucosa; also it is frequently the site of an aneurysmal dilatation.

Salinger and Pearlman have collected the following figures on pharyngeal hemorrhage: Out of a total of 227 cases of hemorrhage, there were 159 in which no ligation was done and of which only 36 (23 per cent) recovered. Seventy-two cases were ligated, and forty-seven recovered (65 per cent). There were 18 ligations of the external carotid with 11 recoveries (61 per cent), and 54 common carotid ligations with 36 recoveries (67.5 per cent). The vessel most frequently involved was the internal carotid artery. Twenty-five per cent of all common carotid ligations are accompanied by serious cranial complications at least one-half of which are fatal. The serious brain complications are due to the sudden shutting off of the arterial supply to half of the brain.

Where successive hemorrhages occur due to the erosion of a large vessel by a retropharyngeal abscess, the presumption is that the source of the bleeding is the internal carotid artery.

PROPHYLAXIS AND TREATMENT OF UPPER RESPIRATORY INFECTIONS

In considering the prevention of the upper respiratory infections, the interest in the subject of "hardening" children has recently been revived; however, it is not a new theme. It has been discussed by the ancients as well as the moderns. Rheum and catarrh were favorite topics discussed by the old Grecian masters. Wadd in his little book *Nursery Mems*—1829, speaks of the fashion then in vogue of hardening children or as he calls it, "Inuring children to hardiness." The practice consisted of dipping the child into ice-cold water every morning. Needless to say this practice caused the children great suffering and piteous crying. This system of hardening was succeeded by the so-called "coddling system." Instead of being plunged into the cold water they were stuffed with food. Thick paps were given in large quantities at frequent intervals, and then flatulence occurred. This was supposed to be due to emptiness, and they were fed still more. Now Godfrey's cordial, now Dalbey's carminative were given to blow away the wind. In the same way calomel was given sometimes in five-grain doses, and repeated frequently, but Wadd, the commentator, says, "all without success." Wadd decried the excessive use of calomel and thought that many were over-calomelized. He calls attention to the serious and somewhat fatal consequences attendant upon the imprudent use of strong medicines. He emphasizes particularly the abuse of antimony and mercury.

J. F. Williams[1] remarks that limitations imposed by the weather cause people to lead unhygienic lives during the winter. For many persons it is a period of semihibernation. Elsworth Huntington[2] says the most stimulating quality of man's environment is a mean temperature between 38° and 64° Fahrenheit. Where it remains above 64° F. all or nearly all the time, or below 38°, human progress is much retarded. Ogle and Mills[3] at the University of Cincinnati found that animals adapted to constant heat, lost to a considerable extent their ability to produce heat and keep warm under chilling emergencies. A few hours of cooling each day is shown to overcome the depressing influence of a hot environment.

By hardening is understood the production of an increased resistance against colds by various measures. Young animals and plants are very susceptible to the influence of colds. It may be assumed that infection and exposure to cold are common causes of upper respiratory catarrhs. Just what the relationship of these factors is, is not known. Some one has suggested that the dynamic equilibrium between bacteria and the defense reactions of the body becomes disturbed by chilling,

and infection results from the production of vasomotor disturbances. Ivan Rosenstern maintains that children exposed to fresh air treatment systematically develop a resistance to cold, though he believes that individual constitution is of importance in resisting the affection. His method consists of systematic fresh air treatment combined with exposure to cold or ultraviolet ray.

Children who had been previously susceptible to recurring catarrhs responded favorably to fresh air treatment. He admits that a small number of children have "colds" in spite of the hardening process. He thinks these children have a constitutional susceptibility to infection. Other factors must be taken into consideration besides fresh air treatment, such as nutrition, hygienic care, medication, the proper diet with an adequate supply of vitamins, and the acid-base balance.

It should be noted that the influence of the same degree of cold and exposure calls forth different reactions in different persons. Marchand considers the predisposition to colds as an individual hypersensitiveness or as a deficient resistance. In other words, a certain abnormal tendency of the body must be present for the development of illness after exposure to cold, though cold cannot be considered the sole causative factor. Predisposition, exposure, and infection seem to be associated in some way, whether anomalies of the circulatory apparatus or the much maligned autonomic nervous system are the fundamental factors is also not known. It has been further suggested that the cold may damage or paralyze the cilia of the epithelial cells in the upper respiratory tract. Or as some have thought, the cold may lead to fissures or tears in the surface epithelium of the trachea and lungs.

The child should be clothed so as to be kept comfortably and sensibly warm. He should be protected against local chilling, as well as against cold, wet feet. If his garments become wet or cold by rain or snow or by a fall into a puddle, he should be taken home to have his clothes removed.

If it is found that a child perspires profusely when out of doors or at play, he is dressed too warmly. If he is chilly, he needs more clothing. The temperature of the average American home is subject to considerable criticism by foreign visitors. They say that in the winter time the air of the room is too hot and too dry. Of course it must also be added that Americans abroad complain of their inability to keep warm in cold, damp rooms. Whether there are more colds in America or abroad is a riddle which the statisticians have not yet charted.

MEASURES TO PREVENT INFECTION

A few general statements for the prevention of infection may be briefly enumerated. It is known to every practitioner that during the severer seasons of the year, colds and so-called upper respiratory infections occur in epidemic form throughout the community, in private homes, and in institutions. When a child, an attendant, or a parent falls ill with a cold he should be isolated from other members of the group, and the infant or child should be protected against those who are acutely ill with an upper respiratory infection. Those who have colds and come in contact with the child should wear masks. Respiratory infectious disease is communicated from one person to another by droplet infection, propelled by explosive coughing or sneezing from the sick person. Assemblies of large numbers of persons in schools, theaters, and railroad coaches are distributing points for spreading colds and respiratory infections. The hands should be frequently washed, especially before mealtime, so as to avoid carrying the infection with the food.

Rooms should be cleaned with a vacuum cleaner instead of the old fashioned feather duster. The latter does not remove the dust, but scatters it with its germs through the room. During an epidemic, whether it be in the home or in the hospital, face masks should be worn by persons coming in contact with the sick, as well as those who are convalescing from respiratory infection. Linen, handkerchiefs, and

towels used by those who are suffering from nasal or oily discharges are filthy, unhygienic, and archaic. When replaced in the pocket, they infect the clothes of the carrier and when withdrawn scatter the contagion. Paper handkerchiefs, which should be burned, are preferable. Everything should be done to keep the mucous membranes of the nose, pharynx, and accessory nasal sinuses in a healthy condition. This includes the removal of infected tonsils and adenoids.

THE USE OF "COLD" VACCINES

This form of prophylactic treatment has been extensively employed, vaunted by some, and rejected by others. Since no one definitely knows the specific cause of colds and upper respiratory infection, it is difficult to understand how a specific vaccine can be produced. In this connection we may quote from a recent paper of Dochez and his associates, who summarize the results of vaccine treatment by stating that they believe many of the pathogenic organisms found in the respiratory tract are secondary invaders. They believe the results obtained by treatment of colds with vaccines vary only slightly in the vaccinated and the nonvaccinated groups. They say that if the thesis is correct that the common cold is due to a filtrable virus, no results from vaccine would be expected.

Attempts to immunize infants and children against colds have also been employed. The vaccine was given at weekly intervals over a long period of time; however, Dochez and his workers found there was no reduction in the occurrence of the number of simple colds or of respiratory infection associated with fever in the vaccinated as compared with the nonvaccinated groups. They believe, however, that there may be an apparent reduction in the severity of the infections in the vaccinated infants if a shorter duration of the fever may be accepted as a criterion. Their general belief is that even vigorous vaccination against the organisms identified in these infections offers incomplete protection.

THE TREATMENT OF UPPER RESPIRATORY INFECTIONS

Acute Nasopharyngitis.—The child suffering from an acute nasopharyngitis with or without fever, preferably should be put to bed. The room should be ventilated; it should be neither too hot nor too cold. Fresh air is of undoubted value. The windows should be open for a time at least each day. Under properly conducted fresh air treatment the child becomes quieter; the appearance improves; circulation stabilizes; the respiration becomes more quiet; and he is less restless, and sleep is induced.

The question of the treatment of the nasal discharge and the swollen nasal mucosa varies in the opinion of the practitioners. The use of the silver solutions, such as argyrol, sylvol, and protargol, is widespread. Nearly every mother and nurse has a bottle on the shelf. It is certain that the uncontrolled and continued use of these preparations has caused argyria in some instances. In addition, these preparations may be irritating to the nostrils and are of doubtful value. The menthol, eucalyptol, thymol, camphor preparations, whether as an oil or ointment, may give temporary relief. However, in the end they may be irritating while the relief is only subjective. There is always the danger of forcing secretions into the eustachian tube if the oily preparations are used with considerable force. Recently we have been cautioned against the possibility of aspiration pneumonias from the instillation or the aspiration of oil into the bronchi. The preparations of ephedrin and adrenalin in solution or in ointment, or the instillation of normal salt solution, or boric acid solution, frequently give relief. The doctors of a generation ago used mild sugar solution, a practice which has been revived in some quarters.

When the patient is in bed, he should be kept on a bland nonirritating diet with a measured amount of milk, a low protein and a moderate carbohydrate diet. The

citrus fruits, and other stewed fruits, honey, jellies and syrup on bread, in moderation, and water in abundance. The room should be kept moist. This is best done by soaking large turkish towels in warm water and hanging them on a line, or large clothes horse, and sprinkling small quantities of oil of eucalyptus or turpentine on the wet towels. This method supplies a pleasant moisture to the room and in my opinion is far superior to the boiling steam kettle, which makes the room hot and stuffy, most often uncomfortable. These acute upper respiratory infections are frequently self-limited and over-treatment is not required or desirable. On the other hand, complications, which have already been referred to and which may require special attention, may occur.

TREATMENT OF SINUS INFECTIONS

The use of hypotonic salt solution to free the nostrils and the nasal mucosa of discharge will in some instances reduce the swelling of the nasal mucous membranes and promote drainage from the sinuses. The value of irrigation or suction of the sinuses in the acute or hyperacute stages is doubtful; indeed, these procedures may do harm in this stage. Where the sinus infection goes on to protracted stage, surgical drainage of the affected sinuses will become necessary. Quartz lamp treatment during the winter or a change to a warm, dry climate may be recommended. Vaccines are recommended by some and disapproved by others. On this point the final word has not been spoken although one cannot help saying out loud, "If you do not know the specific organism, how can you prepare a specific remedy?" Or perhaps by some hit or miss method we are using some vaccine which may contain an unknown specific antigen.

As for the treatment of the associated lymphadenitis, nothing new can be recommended. The ice-bag externally—in the later stages several mild x-ray treatments given about a week apart cause the glands to diminish in size and eventually to disappear.

Tracheitis is treated by inhalations, warm drinks, and sedatives for the irritating and disturbing cough.

If the upper respiratory affection is due to an allergic condition, its cause and nature should be ascertained either by the elimination method or by skin tests and an appropriate regime and management, either dietetic or by removal of the offending allergen.

I shall not enter into a discussion of the treatment of the remaining disorders of the upper respiratory tract, as, except in the case of diphtheria, there is no specific treatment. In considering laryngitis and bronchitis, the treatment is in the first instance, prophylactic, finally expectant and symptomatic; and while there is considerable individual variation as to the methods employed, all are agreed that these affections in the vast majority of the cases, are self-limited and that a rational therapy without overdoing, careful management, without neglecting the cardinal symptoms of hygiene and common sense, will in the majority of cases offer the most efficacious plan of treatment. And it is also true that infection of the ear and mastoid, abscess formation in the pharynx, hemorrhage due to ulceration into a large vessel, as well as infection of the accessory nasal sinuses will frequently require the aid of the surgeon or the otolaryngologist.

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DISCUSSION

DR. HORTON R. CASPARIS (NASHVILLE, TENN.).—This is a difficult subject to discuss and you probably know much more about it than I. I am supposed to discuss the etiology, bacteriology, and immunology of upper respiratory infections.

One phase of this subject in which all of us are interested is the general predisposition or general immunity to respiratory infections. We are beginning to feel that the general health has a good deal to do with this. It is difficult to prove that if the child's general nutrition and health are maintained at a high level, he may not be particularly less subject to infections of the upper respiratory tract, but he seems to recover more rapidly. How much importance can be attached to the value of the use of vitamin A is not known. A good deal of work has been done to determine whether vitamin A specifically helps to prevent these infections of the respiratory mucous membranes. This has not been satisfactorily proved, but it seems that animals on diets deficient in vitamin A are more subject to these infections.

It is also difficult to tell just what conditions are going to induce clinical manifestations of an upper respiratory infection because we know that during an epidemic infection any one may be a victim regardless of the nutritional state or the health. There are, of course, such conditions as exposure to cold, poor nutritional state, etc., which will produce trouble. Those are things we should learn more about.

From a bacteriologic standpoint, all we can say about the etiology of an infection is that there are certain organisms which figure prominently in these infections. Streptococci are probably the commonest although they are not always demonstrated. There may be present also influenza bacilli, pneumococci, and occasionally staphylococci. The work of O'Shea and others shows that staphylococci are not commonly present in these infections. Just what part these organisms play in initiating the infections we do not know. Is it something that happens to the patient, which gives these organisms a chance to take hold? Is it a congestion of the mucous membrane as a result of irritation? Is it exposure to cold? Is it poor nutrition? Is it blocking of the paranasal sinuses, or do they play just part of the rôle? Are the filtrable viruses, as suggested by Dochez, the primary cause and the organisms secondary?

In these conditions, we must differentiate between allergic states, respiratory and actual infections. If there is swelling of the mucous membrane and the sinuses are blocked off, any organism that happens to be there seems to have a better chance to cause trouble. I think sometimes the cart is put before the horse and the paranasal sinuses are blocked off because of the infection. Pus, which will come out later, will form, and then it is said the organism caused the sinus infection. However, these organisms can enter regardless of whether there is anything to cause it if there is a favorable condition in the mucous membrane.

From the standpoint of infection, the paranasal sinuses can be considered also and they are frequently involved. It has not always been known that the sinuses appear as early in life as they do. The maxillary sinus is sometimes present at birth though it has not developed very much. The frontal sinus appears between the ages of two and four years. The ethmoid sinus is present at birth and its development is gradual. The sphenoid sinus usually appears a little later, coming about the age of from three to five years. The mastoids are present always and form the most common site of involvement in the younger child.

In speaking of the immunologic response of these children, it is not known how much immunity can be built up in any individual case. We have felt that some infections may recur and help to build up an immunity in some cases. We have also felt that the tonsils are a means of building immunity to these infections. The adenoids may play some rôle, as well as the sinuses. Just how much we can help

these patients by artificial means is difficult to say. Children who are particularly subject to upper respiratory infections and have colds all the time may belong to the allergic group.

For example, we saw an eight months old child with colds since birth. His nutrition was fairly good; he was not very pale and not noticeably affected by these repeated infections. We found the child had a typical hay fever. The hay fever causes congestion, and a secondary infection may complicate the picture. We found this child sensitive to certain things, which were eliminated, and the repeated infections have disappeared.

One thing that helps in making a differential diagnosis in these children is that they rub their noses a great deal, when there is an allergic condition.

The value of attempts to immunize by means of cold serum and autogenous vaccines from the organism present in the sinus infection is difficult to determine unless a large series of cases is studied. When the diet of these patients is improved, we get some response because of an improvement in the general condition. I mention that in connection with immunologic response.

We are all interested in the question of tonsils. I believe tonsils are very valuable in building up immunity, especially in younger children, against the common organisms that invade the upper respiratory tract. It is very difficult to decide when to remove tonsils unless they are manifestly very bad. For instance, a history of repeated attacks of tonsillitis, the appearance of the tonsils and being able to express grayish material does not mean they are bad. Crypts of the tonsils are a normal part of the tonsil surface, and if these are gone, I become very suspicious. If, in a case of repeated attacks of infection, the anterior pillars of the pharynx about the tonsils are dull red and most of the crypts walled off, I then decide those tonsils should come out. I think we have removed enough tonsils to say that good results have been obtained in those cases in which the tonsils were definitely retarding factors, but we must also admit that many times tonsils have been removed without accomplishing much. They should not be removed before the child is four or five years of age if it can be avoided.

I had a patient with an attack at the age of twelve months. The child kept having red tonsils with exudate and a high leucocyte count. He would be free of symptoms for about three weeks and then have another attack. At the age of twenty months we decided to remove the tonsils. They were not large and when we took them out, they contained no pus but all the crypts were sealed over. We removed the tonsils months ago, and he has progressed nicely.

DR. C. C. RUDOLPH (ST. PETERSBURG, FLA.).—Is there any value in treating these cases of upper respiratory infections by swabbing the throat?

DR. CASPARIS.—I feel it does no good so far as the disease itself is concerned.

DR. RUDOLPH.—Would it sometimes do harm?

DR. CASPARIS.—It helps the mother, but I do not believe it helps the child. It frequently makes the child much more uncomfortable, and I believe there is no advantage in the treatment. I think you cannot reach the causative factor by swabbing. If you apply mercurochrome and then look at the place swabbed, in a short time you will find that the mercurochrome is gone.

DR. RUDOLPH.—If these patients go to an eye, ear, nose, and throat man, that is the first procedure.

DR. CASPARIS.—I had a patient come in a short time ago from her nose and throat man. I asked her if she thought I could prevent colds by swabbing the throat. She said her doctor periodically does this and he can stop colds at any time if she will come in immediately she notices any symptoms.

DR. F. S. CLARKE (OMAHA, NEB.).—You intended, it seemed to me, to show that in most of your cases of upper respiratory infections the child was not healthy. In my opinion, at least 50 per cent are healthy children.

DR. CASPARIS.—I did not mean to give that impression. I wanted to say that the healthy children are not as badly attacked by these infections since the healthy child recovers from them in better condition.

DR. RALPH M. TYSON (PHILADELPHIA).—You spoke about the diet in building up the general health. Do you believe an excess of carbohydrate food, which is the cheapest food, has anything to do with making the mucous membrane more susceptible?

DR. CASPARIS.—These children who are fed an excess of carbohydrate give the impression that they seem to be more susceptible and do not do as well if they get an infection.

DR. TYSON.—I wondered whether it was the excess of carbohydrate or imbalance of the diet which gave this impression.

DR. CASPARIS.—I do not know.

DR. ELMER L. TIMMONS (COLORADO SPRINGS, COLO.).—You do believe that where there is an enlarged tonsil and a severe infection, a child may go on without the tonsil being removed?

DR. CASPARIS.—I think there is more to a bad tonsil than its being large. A history of attacks of tonsillitis is important. I would be inclined to let a healthy child go on who is getting along nicely, even though the tonsils are enlarged, and there is nothing else much except the enlarged tonsil. We have followed some of these patients for six months, trying to decide whether the tonsils were causing the trouble. They were undernourished and had a poor appetite. When the tonsils had been removed, they would gain five or ten pounds in the next month or so, and we have the impression after such experiences that that type of tonsil was a handicap. I use everything at my disposal to decide whether the tonsils are handicapping the child. I believe tonsils are very beneficial but just as soon as they get to be a handicap, then is the time to remove them. Being able to decide that is not always easy.

DR. TIMMONS.—I have had the same experience but when these children fall into the hands of an enthusiastic throat surgeon, they are persuaded to have them removed. I can recall about six cases of this type. The tonsils were not handicapping the child. I have seen these children recently and they have not been hurt by the tonsils.

DR. ARTHUR ABT (CHICAGO).—Do you think hypertrophy of the tonsils can cause deformity of the mouth and jaw?

DR. CASPARIS.—I think deformity is more apt to be caused by the child's poor general nutritional state. Rachitic children with weak muscles and bones that are not developed are more apt to have trouble. I suppose some deformity might develop from hypertrophy especially when the adenoids are actually blocking the nasal passage. This brings up the question of thumb-sucking. I have seen so many children who have sucked their thumbs for three or four years with perfectly good mouths that I think there is more to it than partial obstruction.

DR. TYSON.—Are the endocrine glands active in developing immunity?

DR. CASPARIS.—I would like to have your opinion on that.

DR. TYSON.—It seems to me that children develop an immunity against colds at about the age of six. From the age of six to nine years, they are not subject to colds any more. I have wondered whether the sex glands are more active and stimu-

late a general and natural immunity or whether the repeated attacks of infection produce a specific immunity.

DR. CALVIN E. BRADLEY (TULSA, OKLA.).—One etiologic factor overlooked by the average pediatrician is the bed and sleeping room of the child. I think these patients develop immunity to colds because they grow older and are transferred to a larger bed. The crib of an average child will have a mattress like a comforter and over it will be piled blankets and covers. Parents forget that cold air comes up underneath the child and his resistance is lowered.

When the child is put to bed, the windows are opened allowing the breeze to come in, and there is a tendency for the child to chill especially when he is quite inactive. It will undoubtedly produce irritation of the mucous membrane of the respiratory tract.

The humidity of the room also is not constant. Sometimes the room will be overheated, and the air becomes very dry. The mucous membrane does not secrete an amount of mucus sufficient to protect against invasion of organisms. There is a source of constant contamination from other members of the family who have chronic sinusitis and cough in the face of the patient.

DR. CASPARIS.—Humidity is a factor that has a great deal to do with the vulnerability of the mucous membrane of the upper respiratory tract. The mucous membrane is protected by the secretion of mucus. I think people will have more tendency toward infections if they live in houses where there is overheating and drying of the air.

Most people do not realize that infants and small children do not need as much cover at night as the adult because they maintain their body heat much better. The average child does get out from under his covers, but he is often wet with perspiration when he does and gets a chill. If the average child uses half the amount the adult does, this may have something to do with protecting him from getting a chill if he crawls out from under his covers.

Swimming in pools is another important factor, as most of the water in these pools is chlorinated. Persistent infections occur in children who swim a great deal. Some nose and throat men say that the human body is not built for water and that we should never swim. That is pretty hard. Yet, there is no doubt that these children are taking a chance of getting severe infection from the water carrying organisms into the sinuses.

DR. NICHOLSON (PHILADELPHIA).—How often do you x-ray children with these recurring colds?

DR. CASPARIS.—X-ray examinations have to be very good to get much information other than a very marked sinusitis. In the usual x-ray in which we cannot see the soft tissues, we cannot tell much about the findings. You can tell also by the nasal discharge and whether or not the child seems to be retarded by the infection. There is always some sinus infection in these recurring colds and if they persist and the child does not improve, involvement of the sinuses must be suspected.

DR. JULES M. BRADY (ST. LOUIS).—Dr. Casparis mentioned vitamin A but nothing has been said about vitamin D. I recall the day when upper respiratory infections were a regular plague and many babies died of bronchopneumonia. Some four or five years ago we routinely used ultraviolet rays on all our babies every other day and since that time upper respiratory infections have occurred of course, but they seem to be milder; bronchopneumonia is rare, and I feel this should be emphasized. We gave cod liver oil for years, and the babies continued to have rickets. Now we have abandoned cod liver oil and do not use viosterol; we depend entirely on proper diet and the regular use of ultraviolet rays. We believe this has an effect on reducing the mortality.

DR. CASPARIS.—I would like to emphasize the fact that every one with an upper respiratory infection should stay away from infants.

With regard to vitamin D, I cannot say much. When we had a lot of rickets, the babies were susceptible to bronchopneumonia. It was felt that this was due to lack of cod liver oil and vitamin A. Vitamin D from irradiation may have something to do with it. The men in Baltimore were not particularly impressed by irradiation but their work was in older children.

DR. BRADY.—Our babies get plenty of vitamin A.

DR. CASPARIS.—It is very interesting, and this method of feeding may have something to do with it. We have learned a great deal in the last five years in regard to infant feeding and the effects of vitamins A and D.

DR. NICHOLSON.—Are there any other factors in ultraviolet rays?

DR. CASPARIS.—There may be some very important factor present in ultraviolet rays.

DR. NICHOLSON.—I have found that my babies who do not gain on ergosterol do gain under ultraviolet rays.

DR. FRANK T. MITCHELL (MEMPHIS, TENN.).—For the past fifteen years I have been most interested in the type of sinus infection which should be drained. We have tried to determine the development of the sinus and have observed some 200 normal infants during the first ten days of life to see what sinuses were present. We have found that the maxillary sinus is present at birth, some being larger than others. Our work shows that the shape of the sinus will resemble somewhat that of the parent the child resembles most in general facial expression; also the sinus history will follow somewhat the sinus history of that parent. I might mention an instance of a family where the father was a typical sinus sufferer with very poorly developed sinuses. The mother had normal sinuses and no sinus trouble. A daughter resembled the mother and had normal sinuses while three other children who resembled the father in facial expression, resembled the father also in their sinus history.

The sphenoid sinuses do not develop much before the fourth year and continue until the child is about ten years old, at which time the development of the sinus is complete. The ethmoid sinus is present at birth and develops until the child is twenty-five years old. The frontal sinus begins to develop about the eighteenth month and continues to develop until some time about the fourth year. I think it is fairly well accepted now that the frontal sinus develops as a result of a migration of cells from the ethmoid to the frontal bone.

We believe if one suffers from a sinus infection early in life, the frontal sinus does not develop. This is coincident with development of the maxillary sinus. If sinusitis is continuously present for some time, there is a retardation in development so that you can tell a chronic sufferer by the development of these two sinuses particularly. We have taken many pictures of adults who have shown no sinus development at all and in whom the frontal sinuses are entirely absent and the maxillary sinuses are halfway down the nose. This is an infantile type of sinus.

In deciding whether a sinus should or should not be drained, we have depended the last few years on the anatomy of that sinus. The sinus is lined with columnar ciliated epithelial cells implanted in the mucous membrane. This works all secretion toward the opening into the nose. If a child suffers from sinus infection, scar tissue will close the opening which discharged the secretions, consequently, something must be done to reestablish this drainage. We recommend a simple drainage through an accessory opening under the turbinate into the nose and injection of a brain broth. That should be the only surgery attempted in the accessory opening of a sinus. We leave in a tube for about four days so that the drainage will continue. We touch only chronic sinuses; we do not ever touch an acute sinus.

If a child eight years of age with infantile sinuses and attacks of sinusitis is sent to Florida, while on the beach he seems to have sufficient drainage so that his symptoms disappear, but when he returns to Memphis the sinuses fill up, and he

again does not have sufficient drainage. Do these children who have sinusitis with infantile sinuses suffer for the rest of their lives or can you re-establish the development which should have taken place? Our experiences have consisted so far in following these cases with a control in this way: We have compared a group of children, eight or nine years of age, with no frontal sinus and a poor development of the maxillary. In some instances, we have operated on those children to drain the sinus and watched the individual child two or three years. At the age of sixteen or eighteen, we have found a normal sinus development. The frontal sinus would be normal, and the child would no longer be a sinus sufferer. In other instances where operation was refused, the children retained their infantile sinuses and had trouble during this period. We believe that if this opening in the maxillary is closed, the children will show the topography of chronic sinusitis. We believe surgical intervention is necessary to re-establish drainage, or these children will suffer year after year.

One other point I would like to mention and hear discussed is: Does the removal of healthy tonsils predispose to sinus infection? Some of the laryngologists say it does not, others disagree. One says definitely that when you remove normal lymphoid tissue which has some purpose, an extra burden is thrown on the remaining lymphoid tissue. I do not see why the tonsil was put there if it is to be immediately removed without any cause.

DR. JAMES G. KRAMER (AKRON, OHIO).—I wonder if you would discuss the different medical procedures?

DR. MITCHELL.—In acute sinusitis, I agree with Dr. Abt, there is no particular treatment other than building up the child generally, supplying the proper food and vitamins. It has been claimed that a red sinus means too much acid in the system; the pale sinus too much alkali. The diet should be regulated along those lines.

In chronic sinusitis, it has been my experience that nothing permanent is accomplished without drainage. I think thorough surgical drainage is the best and is necessary. An accessory opening should be made under the turbinate so that the natural opening will not close.

One other point I should like to make is that we have found the tonsils will continue growing in some cases until about the eighth year, then for some reason they retrogress, and a great many children who have had tonsillitis until that time, if they are let alone, seem to do very well. We have also observed that some children whose tonsils were removed show improvement, but the next year the same symptoms reappear as were seen before the tonsils were removed.

DR. TYSON.—What about the use of transillumination in making a diagnosis of sinusitis?

DR. MITCHELL.—We believe transillumination is of no use. We depend on the x-ray almost entirely in the diagnosis of chronic sinusitis. This means not upon the shadow but upon the topography of the sinus.

DR. TYSON.—Do you think the improper development of the face depends on adenoid enlargement, or is due to changes in the nose?

DR. MITCHELL.—Changes in the nose.

DR. TYSON.—Is the obstruction due more to a nasal condition than to adenoids?

DR. MITCHELL.—I will answer that by saying if the adenoids are removed one winter, the following winter adenoid symptoms will return, and you will find there is also a marked sinusitis.

DR. BRADLEY.—Have you found that patients in whom an adenoidectomy and tonsillectomy have been performed, a chronic postnasal drip develops later?

DR. MITCHELL.—Yes, but we do not know what would have happened if these operations had not been performed. We often see no relief following these operations. We remove adenoids only when they are hypertrophied.

DR. FREDERICK C. RODDA (MINNEAPOLIS, MINN.).—It is fair to assume that our experiences up nearer the north border, where we have both low and high temperatures and the air is very dry, might be different. Undoubtedly, damage is done to the mucous membranes of some of our children. I feel that the production of a certain humidity is a great help but that depends upon how you use it, for the child is in school most of the day, and although there may be the right humidity in the home in the day, it is not present at night. Some form of air-conditioning better than the present form will cut down the incidence of upper respiratory infections.

We have also noticed that when sunshiny days come in March and April when we should expect betterment in the condition of these patients, there is a most vicious type of infection. This may not be so common but the infection is vicious, and it is hard to determine whether the child gets an overdose of sunshine in the first days of spring.

In comparison with conditions fifteen years ago, I think there are two factors which are important; we have better technic and we are more hygienic. We must not overlook the peculiar cycles of infections. If we are going to draw conclusions, we must include a larger cycle than a period of a few years.

DR. ORVILLE E. BARBOUR (PEORIA, ILL.).—In speaking of this late spring infection, I think the element of fatigue plays an important rôle. We all see examples of a lowered resistance and the appearance of infection in late spring. We see a great deal of this toward the end of the school year. I have always felt that the element of fatigue, both mental and physical, entered into the condition. Perhaps, as Dr. Rodda mentioned, the sudden sunshine might be the cause. Stimulation from the sun might be injurious rather than helpful.

DR. ISAAC A. ABT.—I expect that the element of fatigue does have something to do with these late spring infections. It is so difficult to evaluate these different facts as one is so likely to minimize one and overvalue another. Anything that decreases bodily strength I presume decreases bodily resistance.

DR. CHARLES N. KENNON (MIAMI, FLA.).—We have as many respiratory infections in Miami as in other climates farther north; the climatic advantages there are less certain than it would appear. Many a child comes from Chicago for the winter sun and may have as many colds, though possibly less virulent, as he may have in the North and that same type of cold often recurs on his return home. Many children who have been quite uncomfortable with sinusitis go to Miami or the lower coast of Florida and are relieved, but after returning to their homes they have recurrences. We feel that the number of colds is practically the same in Miami as it is in the North.

DR. ISAAC ABT.—Do these patients get too much sun perhaps?

DR. KENNON.—The fact that the native born also have colds makes me feel that something other than the element of sunlight or calcium base metabolism is the important factor. It is an interesting thing that some of the children who are out of doors and get too much ultraviolet rays in the winter complain of headache and marked fatigue. If they put on dark glasses or stay out of the sun, they adjust themselves. This discomfort is accompanied by definite edema of the nasopharynx.

DR. TYSON.—We are all familiar with the experience of going from one city to another and contracting a cold. I am wondering whether this transfer from the North to the South or vice versa is not a question of immunity to a certain type of organism. This immunity is lost for a while, and it is like a new group of organisms, and it is necessary to regain that immunity.

DR. BARBOUR.—Perhaps diet might be a factor. The vitamin and mineral content of the food in Florida is different.

DR. NICHOLSON.—I have used bacteriophage with good results in 100 cases. In none of these cases has there been any operation and successive x-ray pictures

show the sinuses largely cleared up. In some of the cases there were large retentions of pus in the ethmoid sinuses, consequently, I am inclined to believe that if we could reach them in the early stages before they become chronic, we would get better results.

DR. CASPARIS.—Bacteriophage has been used in various types of infection and good results have been reported. We used it in an epidemic of very severe infection, and it did not accomplish anything. Others have used it in mild infections and have had wonderful results. It has been used in dysentery but its use in this condition is difficult to evaluate because we have epidemics of mild and severe infection. With regard to its use in other conditions, the results are varied.

DR. NICHOLSON.—I think the ordinary commercial bacteriophage is useless. The bacteriophage we used was made by a pupil of d'Herelle and the results with this type of bacteriophage were excellent. This is very important in testing the value of bacteriophage.

DR. CASPARIS.—I wonder if there is any disadvantage to lowering the temperature in these infections. It has been suggested that one of nature's methods of destroying the organism is to elevate the temperature. Then we come along and lower it. Theoretically, it places the patient at a disadvantage.

DR. TYSON.—We must remember that the temperature affects children differently.

DR. CASPARIS.—I do not mean to make the patient uncomfortable, but may we not give drugs that give relief without lowering the temperature? Theoretically, if it is nature's means of combating infection, we are putting the child at a disadvantage by taking it away from him.

DR. ISAAC ABT.—It seems to me that temperature has its dangers. There is not much to worry about in a man or child who has a moderate temperature, but we know very well if the temperature ascends there are certain heights that are not compatible with life. Also, the child who has a high temperature loses his appetite, will not drink, is very restless; and one of the good things you do by reducing the temperature is to increase the fluid intake and this makes him more comfortable. He sleeps and is not restless. Some good is done, his distress is relieved, and I do not believe you are doing any harm. In the newborn premature, our great effort is to maintain his temperature. We go so far as to keep the temperature between 80 and 90 degrees. On the other hand, when the temperature is extremely high, we try to lower it or bring him in a cooler environment so that after all the normal temperature is the temperature at which we live best and thrive best and even in disease, it seems to me if you can reduce the temperature moderately we are not interfering with the vital processes. Of course, I am answering this without any thought of the scientific values but of the practical values.

DR. BRADLEY.—What do you consider the best antipyretic? The patients in whom I have used the one you suggested have had nausea, vomiting, and discomfort.

DR. ISAAC ABT.—I think it depends entirely on the patient. Any antipyretic that will do no harm and is borne by the patient is the one to use. I do not think there is any one better than another.

DR. CASPARIS.—Do you consider it unfavorable to see a patient with pneumonia who does not have much temperature response? In other words, is a high fever with pneumonia favorable or not?

DR. RODDA.—I would think a moderate temperature with pneumonia would offer a better prognosis than extreme hyperpyrexia.

DR. ISAAC ABT.—From my own experience, I have seen pneumonia patients with a temperature of 107° F. and over. Those were not the lobar types and would go on to recovery. On the other hand, I have seen little babies with terrifically high

temperatures that continue as terminal temperatures, and the patient died. The summer of 1890 we had a lot of cases of sunstroke. I do not know whether any of you deal with this condition, but these men would fall off their wagons, and the children fell in their play and every hospital in this whole region was treating emergency sunstroke cases. These patients would be brought in in patrol wagons and delivery wagons. We were in the midst of a terrific heat spell. These patients would have temperatures from 109° to 112° F. Those we could get to rapidly and reduce their temperature we could save, but those who were neglected or were a long time coming to the hospital, just burned up, dried up and died. We saved a certain number of them, and it seemed to me that those who were saved were those who were brought in quickly and their temperature lowered by artificial means. It shows what extreme temperature does. What the pathology of sunstroke is, I do not know but at any rate, there is a complete loss of control of heat regulation. As far as pneumonia is concerned, I have seen children with a high temperature, who ran a favorable course.

DR. KRAMER.—I have been using a certain technic in tonsil work which I think is valuable and extremely important. The tonsil is imbedded between the two pillars which are made up of musculature. Normally the tonsil is emptied continually by massage of these muscles, expressing the material out of the crypts. Press the tongue down with a tongue blade and another blade is applied to the pillar laterally. With definite pressure on the anterior pillar, press out infected material, and if you can evacuate the crypts of that material, I should say you have a tonsil that needs to come out.

DR. ISAAC ABT.—But you have other indications.

DR. KRAMER.—I am just adding that to all the other indications.

Academy News

The fourth annual meeting of the **American Academy of Pediatrics** will be held in Cleveland on June 11 and 12, 1934. The program will consist of various round table discussions to be given on Monday, June 11 at 9 A.M., and will be repeated for a second group Tuesday afternoon, June 12 at 2 P.M. These round table discussions will be held at the Wade Park Manor Hotel, the headquarters of the meeting.

General meetings of the Academy will be held on Monday afternoon and Tuesday morning in the Cleveland Medical Library. On Monday morning, Professor Wallgren of Göteborg, Sweden, will address the Academy, and there will be a business meeting. Tuesday morning there will be panel discussions on "Dental Caries" by Dr. F. F. Tisdall and "The Ductless Glands" by Dr. R. G. Hoskins.

The meeting of the Academy will precede the meeting of the American Medical Association.

Hotel reservations should be made directly with the Wade Park Manor Hotel.

The following committee has been appointed to take charge of the program for the annual clinical meeting of Region III of the Academy to be held at Rochester, Minnesota, on October 4 and Minneapolis on October 5 and 6, 1934.

Chairman: Dr. Henry F. Helmholz.

For Rochester: Drs. Amberg and Kennedy.

For Minneapolis: Drs. Huenekens, Rodda, Stewart, and McQuarrie.

Dr. Harold H. Mitchell, 270 Rose Street, Freeport, New York, has been appointed secretary of the Committee on School Health and School Health Education.

Comments

THE Fourth Annual Meeting of the Academy will be held at the Wade Park Manor Hotel in Cleveland, June 11 and 12. The Executive Committee has made several changes which should add to the interest of the meeting. Eight round table discussions will be held in duplicate, on Monday morning and Tuesday afternoon. This will give each member the opportunity to attend two discussions. On Tuesday afternoon two panel discussions have been placed on the program. At the general meeting on Monday afternoon the committee reports will be mimeographed so that only important matters and recommendations need be discussed. In addition to the President's address, there will be an address by Dr. Wallgren of Göteborg, Sweden, who is the guest speaker of the pediatric groups this year. The commercial exhibit tried out for the first time at Chicago last year was so successful from both the exhibitors' and Academy's viewpoint that it will be repeated. In addition some scientific and educational exhibits are planned.

It is hoped the attendance this year will be large. Cleveland is easily accessible to a large part of the Academy membership. Reduced railroad rates may be obtained by registering with convention travel certificate at the A. M. A. meeting. The meetings of the Section on Pediatrics of the A. M. A. will be held on Wednesday, Thursday, and Friday mornings. The two meetings together offer not only an unusual opportunity to listen to and take part in a wide range of pediatric discussions, but the opportunity to greet old friends and make new ones in the field in which we are working. Perhaps after all this is the most important thing to be gained in medical meetings of national societies.

THE following excerpts are taken from an editorial in the *Journal of the American Medical Association*, March 31, 1934, entitled "Certification of Specialists."

"At the last annual session of the American Medical Association a resolution was adopted authorizing the Council on Medical Education and Hospitals to express its approval of such special examining boards as conform to standards of administration formulated by the Council and urging the Board of Trustees to use the machinery of the American Medical Association, including the publication of the Directory, in furthering the work of such examining boards as may be accredited by the Council. Pursuant to that action, the Council is beginning with its task of designating and classifying the specialists of the United States. Arrangements have been made in the publication of the next edition of the American Medical Directory to indicate those physicians who hold the certificates of some of the boards already established, and also to describe the nature of the boards which will be considered acceptable by the Council.

"In the meantime, as a result no doubt of suggestions made at a hearing before the reference committee of the House of Delegates at the meeting in Milwaukee, the certifying boards already established have organized among themselves an advisory board which, it is presumed, will serve to coordinate the activities of the several boards, standardizing their methods of work and advising with them in their operation. The functions of this coordinating board are clearly to aid in the practical operation of the boards rather than to define their methods of work or to sit in judgment on the results of their operations.

"The machinery of the American Medical Association in support of the work of the certifying boards has already begun to function to some extent. The mere description of the boards in the American Medical Directory and the listing of those who hold the certificates is in itself a vital step in making effective the advancement of the specialties concerned. Beyond this, however, the American Medical Association has broadcast over the radio, through newspapers and to some extent through its periodical, *Hygeia*, a description of the certifying boards and a statement as to the significance of their certificates. As information concerning the work of these boards becomes more widely disseminated among both the medical profession and the public, their prestige must grow. Eventually the young man who wishes to make for himself a place in any of these specialties will consider the securing of a certificate by a council-recognized certifying board as the first step in such a procedure. Hospitals will also do well to be guided in their staff appointments by similar qualifications.

"Movements of this type necessarily develop and advance slowly. However, with the qualifications and restrictions that have been outlined, there is reason to believe that the certifying boards will do much to advance the quality of specialistic service available to the people and to the profession of our country."

Erratum

In Dr. Lewis Webb Hill's article, "Erythrodermia Desquamativa," in the April, 1934, issue of the Journal, p. 440, the sentence beginning on line 4 should read:

"Four were cured in from four to six *weeks;* one is at the present greatly improved; and one is not at all improved after two months of this feeding."

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